MODERATED POSTER SESSION

1001 Advances in the Interventional Management of Acute Myocardial Infarction

Sunday, March 18, 2001, Noon-2:00 p.m.
Orange County Convention Center, Hall A4

Noon

1001-201 Impact of Contrast Agent Type (Nonionic vs. Ionic) Used for Coronary Angiography and PCI on Angiographic, Electrocardiographic, and Clinical Outcomes Following Thrombolytic Administration in Acute MI

Sabina A. Murphy, Ajay J. Kirtane, Susan J. Marble, Kristin C. Schuhwerk, James de Lemos, C. Michael Gibson. *University of California San Francisco, San Francisco, CA, Brigham and Women's Hospital, Boston, MA*

The choice of contrast agents during angiography and PCI is a subject of controversy. The goal of this study was to examine the relationship between contrast agent type (ionic vs. non-ionic) and angiographic, electrocardiographic and clinical outcomes after thrombolytic administration. We hypothesized that ionic dye may be associated with decreased tissue perfusion after thrombolytic administration. **Methods:** Ionic or non-ionic contrast was selected in a non-randomized fashion for 90 min. angiography and PCI after thrombolytic administration in TIMI 14 (tPA or rPA vs low dose lytic + abciximab). **Results:** Non-ionic contrast was used more frequently than ionic contrast (69%, n=651 vs 31%, n=296). There was no relationship between contrast agent type and overall patency, rate of TIMI grade 3 flow, or corrected TIMI frame counts (CTFCs) in open culprit arteries at 90 min or post-PCI. Patients receiving ionic contrast had greater rates of Q-wave MI, less frequent complete ST segment resolution (>70%), longer chest pain duration, and slightly but significantly lower ejection fractions at 90 minutes. **Conclusion:** No significant relationship was identified between contrast type & epicardial flow at 90 min. or post-PCI in acute MI. However, ionic dye use was associated with poorer ST segment resolution, greater rate of Q-wave MI, longer chest pain duration, and slightly lower ejection fractions, perhaps as a result of increased microvascular dysfunction or the trend toward increased thrombus burden. It should be confirmed that dye type is balanced across arms of trials & further studies of dye type impact on outcomes are warranted.

	Ionic Dye	Non-ionic Dye	p-value
TIMI 3 at 90min (%)	63.3%	62.4%	NS
CTFC at 90min	34.3±21.6, n=217	36.6±24.4,n=485	NS
TIMI 3 post-PCI (%)	85.7%	89.4%	NS
CTFC post-PCI	27.7±20.1,n=91	26.5±23.1,n=198	NS
EF at 90 min (%)	56.2±16.5,n=122	59.8±14.4,n=322	0.02
ECG Res >70% (%)	41.5%	50.8%	0.04
Q-wave MI (%)	77.0%	55.3%	<0.001
Chest pain duration (hrs)	2.8±5.1, n=255	1.7±3.6, n=550	0.0003
Thrombus (%)	32.2%	27.3%	0.14

12:12 p.m.

1001-202 Is Primary Stenting Better Than Primary Angioplasty in Acute Myocardial Infarction?

Michael M. Zhu, Mahmood Alam, Hal Chadow, Alan Feit, Luther T. Clark. *SUNY Health Science Center, Brooklyn, NY*

Background: Several randomized trials have compared primary stenting with primary balloon angioplasty (PTCA) for acute myocardial infarction (MI). Although stenting has been shown to be better in reducing the need for target vessel revascularization (TVR), uncertainty exists in regard to the relative merits of stenting in post-infarction mortality and the risk of re-MI. **Methods:** We performed a meta-analysis of all the randomized trials published up to August 2000 which compared these two revascularization strategies in acute MI. **Results:** Six randomized trials (FRESCO, GRAMI, ESCOBAR, PASTA, Stent-PAMI, STENTIM-2) were identified through searching the Medline database. They studied a total of 1,728 patients (pts), with 859 pts randomized to stent implantation and 869 pts to PTCA. Of the 6 trials, FRESCO and GRAMI included pts with cardiogenic shock at admission (22 pts). The death due to refractory cardiogenic shock was not included in the meta-analysis. The summary data are shown below. **Conclusions:** Based on the meta-analysis of these 6 trials, primary stenting is found to be superior to primary PTCA mainly in reducing the need for TVR due to re-ischemia. There was also a tendency for lower incidence of re-MI in the stent group during the 1-year follow-up period. A nonsignificantly higher mortality was observed in the stent group. However, this finding was based on small number of end points occurred and the mortality difference between these two treatment strategies needs to be better defined in future trials.

Pooled odds ratios (95% confidence interval) for stenting versus PTCA

	Death	Re-MI	TVR	MACE
1 month	1.42 (0.76-2.65)	0.46 (0.22-0.98)*	0.33 (0.19-0.56)†	0.45 (0.30-0.67)†
0 - 6 months	1.31 (0.73-2.34)	0.66 (0.35-1.23)	0.38 (0.28-0.52)†	0.46 (0.35-0.60)†
0 - 12 months	1.46 (0.87-2.43)	0.67 (0.38-1.19)	0.41 (0.32-0.53)†	0.52 (0.40-0.66)†

*p = 0.05; †p< 0.0001; MACE = major adverse cardiac event (death/re-MI/TVR).

12:24 p.m.

1001-203 Long-Term Outcome and Cost-Effectiveness of Stenting Versus Balloon Angioplasty in Selected Patients With Acute Myocardial Infarction

Jan Paul Ottervanger, Harry Suryapranata, Edwin Nibbering, Arnoud W. J. van 't Hof, Jan C. A. Hoorntje, Menko Jan de Boer, Maywen Al, Felix Zijlstra. *Isala Klinieken, hospital De Weezenlanden, Zwolle, The Netherlands*

Background: Primary angioplasty has been demonstrated to be beneficial over thrombolysis in acute myocardial infarction. Use of stents may have additional benefit, compared to balloon angioplasty. Although the initial results of stenting for acute myocardial infarction have been quite promising, long-term clinical outcome and cost-effectiveness have not been reported. **Methods:** Patients with acute myocardial infarction eligible for stenting were randomized to primary stenting (n=112) or balloon angioplasty (n=115). Primary endpoint was the cumulative first event rate of death, non-fatal reinfarction, or target-vessel revascularization. Secondary endpoints were restenosis at 6 months and cost-effectiveness at follow-up. **Results:** After 24 months, the combined clinical endpoint of death/reinfarction was 4% after stenting and 11% after balloon angioplasty (p=0.04). Subsequent target-vessel revascularization was necessary in 15 (13%) and 39 (34%) patients, respectively (p<0.001). The cumulative cardiac event-free survival rate was significantly higher after stenting (84% versus 62%, p<0.001). The angiographic restenosis of 12% after stenting was lower compared to 34% after balloon angioplasty (p<0.001). Despite the higher initial costs of stenting (Dfl. 21,484 versus Dfl. 18,625; p<0.001), the cumulative costs at 24 months were at least comparable to balloon angioplasty (Dfl. 31,423 versus Dfl. 32,933; p=0.83). **Conclusions:** Compared to balloon angioplasty, primary stenting for acute myocardial infarction results in a better long-term clinical outcome, without increased costs.

12:36 p.m.

1001-204 Is Primary Angioplasty the Optimal Treatment for Acute Myocardial Infarction in Elderly Patients?

Edward J. Kosinski, Bardia Asgari, Maria Capasso, Caroline Lawler, Jeffrey N. Berman, Karl Alcan, Corina Marcu, Kathleen Harper. *St. Vincent's Medical Center, Bridgeport, CT*

Background: Primary angioplasty (PAMI) has emerged as the choice of therapy for acute myocardial infarction. However, elderly patients may have a different short and long-term outcome due to the chronicity of their coronary disease. **Methods:** We retrospectively analyzed a two year (1996-1998) single center experience in which all patients presenting with ST elevation infarct were treated with primary angioplasty. No patients received thrombolytic therapy as part of their treatment. Catheterization, angioplasty and hospital records were reviewed for short-term outcomes (less than 30 days). Long-term results (average 2.6 years) were assessed by patient interviews and hospital record review with 95% complete follow-up. Quality of life assessment was determined in 76% of patients. **Results:** 172 patients comprised the study group with 118 males and 121 patients 70 years of age. Ten patients presenting in profound cardiogenic shock were excluded. Procedure success, as evidenced by post procedure TIMI 3 flow in the infarct related artery, was comparable, with 88% in patients 70 years and 84% in patients 70 years. Global ejection fraction and extent of coronary artery disease was not significantly different between the two age groups. Overall mortality within 30 days was 2.9%. Despite similar acute procedural results, patients 70 years had 1.6% mortality and patients 70 years experienced a 5.9% mortality. Target vessel revascularization by percutaneous coronary intervention or CABG was comparable in both age groups (24.6% in patients 70 years and 23.5% in patients 70 years). Despite similar rates of target vessel revascularization, long term follow-up averaging 2.6 years demonstrated 7.6% overall mortality with 3.2% in patients 70 years and 17.7% in patients 70 years. Quality of life analysis also demonstrated more frequent Class III or IV symptoms in 46% of patients 70 years compared to 31% of patients 70 years. **Conclusion:** Although primary angioplasty for acute myocardial infarction results in excellent short and long-term mortality, the results in elderly patients are alarming. The substantially higher mortality in the elderly warrants reevaluation of current therapies.

12:48 p.m.

1001-205 Acute Myocardial Infarction in Patients With Prior Bypass Graft Treated With Primary or Rescue PTCA in the Era of Stenting

Christophe Loubeyre, Thierry Lefèvre, Yves Louvard, Pierre Dumas, Jean-François Piéchaud, Marie-Claude Morice. *ICPS, Quincy, France*

Background: Limited data are available on the outcome of primary angioplasty in patients with prior coronary artery bypass grafts. The role of stents in this setting has not been reported so far.

Methods: Since 1995, in our institution, primary angioplasty has been the only reperfusion therapy for acute myocardial infarction (AMI) and patients are directly admitted to the cath-lab. Until Jan 2000, of 1030 consecutive pts admitted within 12 hours of AMI, 35 pts had prior bypass (3.4%). Stents were implanted directly when possible, and use of GP IIb/IIIa inhibitors, Urokinase, Hydrolyser was at the operator's discretion. Except for radial access (4 pts), a closer device (Techstar) was used for hemostasis.

Results: Mean age was 64 ±11 years. Prior myocardial infarction was reported in 15 (43%) pts. Cardiogenic shock was present in 8 (22%) pts. Four (11%) pts received thrombolysis before admission. Mean time from symptom onset to admission was 229 ± 162 min. The infarct vessel was a native artery in 21 pts and a saphenous vein graft (SVG) in 14 pts. Stents were implanted in 28 pts (78%). Door to stent time was 46±40 min. Abciximab was used in 7 pts (6/7 for SVG), IC Urokinase in 2 pts (SVG), Hydrolyser in one. IABP was inserted in 8 pts. Angiographic success was achieved in 94.3% of pts (100% in SVG), with TIMI 3 grade flow in 85.7% (78.6% for SVG). No major bleeding occurred and

no repeat PTCA or emergency CABG was reported. Reinfarction occurred in one pt. In-hospital mortality was 25% (28.6% for SVG). In non shock pts mortality rate was 11.1%. Median stay duration was 7±5 days.
Conclusion: 1. Although rare, pts with prior bypass represents a very high risk primary PTCA population. 2. In the era of stenting, procedural success can be high, even when infarcts vessel are SVG. 3. Efforts must be carried out to increase TIMI 3 grade flow, especially in cases of SVG occlusion.

1:00 p.m.

1001-206 Primary Angioplasty in Patients With Acute Myocardial Infarction and Multi Vessel Disease. One-Year Outcome After Single Vessel Versus Multi Vessel Angioplasty

Helmut Schuhlen, Adnan Kastrati, Josef Dirschinger, Albert Schomig. *1. Medizinische Klinik rechts der Isar, Munich, Germany, Deutsches Herzzentrum, Munich, Germany*

Background: Standard strategy for primary angioplasty in acute myocardial infarction is PTCA of the infarct-related artery, even in patients with multi-vessel disease. However, ischemia in multi-vessel disease may be induced by multiple arteries, especially in patients with myocardial infarction complicated by cardiogenic shock. A strategy of a more complete revascularization has not been tested in this setting. **Methods:** We performed a retrospective analysis of the one-year follow-up of 439 patients with multi-vessel disease and acute myocardial infarction; 73 of these patients were in cardiogenic shock before PTCA. PTCA of only the infarct-related artery was performed in 364 patients (single-vessel), multi-vessel PTCA was done in 75 patients. **Results:** Angiographic success was achieved in 95.9% in single vessel, and 97.3% in multi-vessel PTCA. The event rates during follow-up are illustrated in the table below. There were no significant differences between the two strategies, neither in patients with or without cardiogenic shock. However, in both groups there is a trend for a higher mortality with multi-vessel PTCA in the first 30 days which is reversed after one year.

		after 30 days		after 1 year	
		single-vessel	multi-vessel	single-vessel	multi-vessel
no shock	death	2.8	4.3	7.8	6.4
	nonfatal myocardial infarction	1.6	2.2	3.1	2.2
with shock	death	46.7	50.0	64.4	60.7
	nonfatal myocardial infarction	0.0	7.1	5.6	9.1

Conclusion: Multi-vessel PTCA in patients with acute myocardial infarction and multi-vessel disease is feasible and can be achieved with a similar high angiographic success rate. This retrospective analysis did not reveal a significant difference between the two strategies during long-term follow-up. However, an initial trend for a higher mortality within the first month after multi-vessel PTCA is reversed after one year.

1:12 p.m.

1001-207 Adjunctive Thrombectomy Combined With Stenting for AMI: The Endicor X-SIZER AMI Registry

David A. Cox, Thomas Stuckey, Reggie Low, Louis Cannon, Robert Iwaoka, Alexandra Lansky, Gregg Stone. *Mid Carolina Cardiology, Charlotte, NC, Lennox Hill Hospital, New York, NY*

Background: Acute MI is typically caused by plaque rupture followed by thrombotic occlusion. Primary PTCA and stenting in AMI may result in distal embolization and microvascular obstruction and reduced TIMI flow. The Endicor X-SIZER Catheter System is a novel percutaneous thrombectomy device employing a helical cutter with vacuum-assisted debris removal. Its utility for treating thrombotic lesions in patients with AMI is currently being evaluated in a 100 patient multicenter registry. **Methods:** 100 patients presenting within 24 hours of AMI will be enrolled in this registry, with all patients undergoing thrombectomy with the Endicor X-SIZER device before stenting. **Results:** To date, 24 patients with AMI have been enrolled with data presently available in 11 patients. Baseline features include mean age 56.1 years, 87% male, and 13% with diabetes. The target vessel was the RCA in 50%, LAD in 25%, and SVG in 25%; all vessels were thrombotically occluded with pre-procedure TIMI 0-1 flow. The reference vessel size was by protocol 3.0-5.0mm by visual estimate (mean 3.7mm). The culprit lesion was completely crossed with the X-SIZER device in 10/11 patients (91%), and partially crossed in 1 patient. Following X-SIZER passage TIMI 2-3 flow was restored in all patients: distal embolization was seen in only 1 patient and no dissections or perforations were noted. All lesions were stented resulting in TIMI-3 flow in all but one patient in whom TIMI 2 flow was present. No patients had thrombus present at the target lesion. All patients were discharged with 0% MACE (death, stroke, reinfarction, or target vessel revascularization).
Conclusion: This preliminary experience demonstrates that X-SIZER use as an adjunct to percutaneous intervention is save and effectively removes thrombus. Data from the complete 100 patient cohort, including quantitative and qualitative core lab angiographic results (TIMI flows, myocardial blush, thrombus burden, etc.) will be available in March 2001.

1:24 p.m.

1001-208 Lack of Intracoronary ST Segment Elevation Resolution Predicts Absence of Infarct Zone Recovery After Primary Stenting in Acute Myocardial Infarction

Vruyr Balian, Sergio Repetto, Marcella Luvini, Franco Galdangelo, Ettore Petrucci, Mauro Boscarini, Battistina Castiglioni, Sergio Ghiringhelli, Michele Galli, Raffaella Vaninetti. *Ospedale Circolo Fondazione Macchi, VARESE, Italy*

Background: During acute myocardial infarction (AMI), >50% ST-segment elevation resolution (STER) after epicardial recanalization both with thrombolysis or balloon angioplasty is a reliable ECG marker of myocardial reperfusion and predicts LV recovery. Intracoronary (IC) ECG is a more sensitive marker of local ischemia as compared to surface ECG. **Methods:** We recorded IC ECG and 12-lead surface ECG in 42 pts with first AMI undergoing primary stenting <12 hours from symptoms onset, and correlated the ECG findings with the degree of late recovery of the infarcted area. All pts had TIMI flow grade 0-1 of the myocardial infarction (MI) vessel, successful stenting (TIMI 3, residual stenosis <20%), and TIMI 3 flow at 6-month angiography. IC ECG was recorded proximal to the vessel occlusion, distal (baseline ST elevation), and 30' after a stable TIMI 3 flow restoration; surface ECG was recorded before reperfusion and 3 hours later. ST segment elevation was measured 20 msec after the J point and STER was defined as >50% decrease of ST elevation from baseline. All pts (59+/-11 yrs; 71% anterior AMI; ischemic time=194+/-72 min) underwent echocardiography soon before procedure and 6 months later. Infarct zone Wall Motion Score Index (WMSI) was derived. **Results:** IC ST elevation was absent proximal to vessel occlusion in all and > 4 mm distal in 37/42 pts. After stenting, IC STER was present in 33 pts (79% group A; from 9,3 +/- 8,8 mm to 1,5 +/- 2,5 mm) and absent in 9 (group B; from 9,1 +/- 4,8 mm to 6,7 +/- 1,9 mm). On surface ECG, STER was present in 29/33 (87%) group A and in 1 (11%) group B . Mean ischemic time was 201 +/- 103 vs 271 +/- 108 min (p=.05), peak CK 2706 +/- 2266 vs 4886 +/- 4111 U/l (p=.08). At 6 months LVEF was 48 +/- 7 vs 37 +/- 9 (p=.003), WMSI decreased from 2,2+/-0,3 to 1,7+/-0,4 in group A, but not in group B (from 2,2+/-0,4 to 2,2+/-0,5; p<.001).
Conclusions: Intracoronary ST elevation monitoring during primary stenting is a readily and inexpensive tool to assess myocardial reperfusion after MI vessel recanalization and predicts late WMSI recovery. Thus, it allows prompt identification of pts without tissue reperfusion who need additional therapeutical interventions (i.e. GP IIb/IIIa inhibitors, adenosine, verapamil).

1:36 p.m.

1001-209 Impact of Operators Skill on Direct PTCA Outcomes in Acute Myocardial Infarction. A View of the SOLACI Registry

Costantino Costantini, Sergio Tarbine, Euardo Sousa, Alberto Sampaolesi, S. Silva, C. Gosttchall, Alfredo Rodriquez, M Martinez Rios, G Bonzon, Espedito Ribeiro, F Tortoledo, Gregg W. Stone. *Clinica Cardiologyca C. Costantini, Curitiba, Brazil*

Background: Primary PTCA is one of the most effective reperfusion strategies for the treatment of acute myocardial infarction. A wide range of results have been showed in randomized trials comparing this technique with other type of treatment. With the aim of analyzing the importance of skilled operators in the outcomes of this method in a medium like ours, we analized the results of this retrospective registry with the participation of 68 Latin American centers members of SOLACI.
Methods: Since November 1982 and up to June 1997, 6793 procedures were reported. 76.3% of patients were male, 43.9% had anterior wall MI, 45.8% had multivessel disease and 28.9% was in Killip class III, IV, and non-standard. 4.2% of the culprit vessels was saphenous vein graft, 7.6% of the procedures was rescue PTCA and only 15.1% used stenting. No IIb/IIIa inhibitors were used. Three groups were analized: centers with < 100 patients (pts), 100-200pts and > 200 pts
Results:

Patients	<100	100-200	>200	P value
Mortality(%)	8.7	9.1	6.7*	0.009
Reocclusion (%)	4.5	4.1	2.8*	0.0001
Final TIMI 3 (%)	83.0	85.5*	84.6	0.0017

Global in-hospital reocclusion had an incidence of 5.3%, 3.5% needing complementary CABG. Regarding the functional class at discharge, 92.5% of the cases was in class 1 of the NYHA classification
Conclusion: This method of reperfusion is being used in numerous centers by adequately trained personnel, the general results obtained being comparable to those of other studies. We must stress the need of a training curve, demonstrated with even better results obtained in more experienced centers (mortality 6.7%, reocclusion 2.8%) as pointed out in trials as PAMI (mortality 3,0 %, and GUSTO IIb PTCA arm (mortality 5.7%).

1:48 p.m.

1001-210 Predictors of Door-to-Balloon Delay in Primary Angioplasty

Brad G. Angeja, Richard Chin, Priscilla Hsue, Paul D. Frederick, Nathan R. Every, Allen M. Ross, Hal V. Barron, C. Michael Gibson, National Registry of Myocardial Infarction 2-3. *University of California, San Francisco, Cardiovascular Research Center, George Washington University, Washington, DC*

Background: Delay in reperfusion increases mortality in acute myocardial infarction. Predictors of delay have been described for thrombolysis but not for primary angioplasty (pPTCA). **METHODS:** Using data from 40,017 patients in the National Registry of Myocardial Infarction 2-3, we calculated median door-to-balloon times according to measured characteristics and determined independent predictors of delay using logistic regression. Comparisons were made to patients without the characteristic. **RESULTS:** Median delays (hour) were longer in older (2.0 vs. 1.8), female (2.0 vs. 1.8), and non-white patients (1.9 vs. 1.8), in those with complicated medical histories, and with pre-hospital delay (2.0 vs. 1.8) or lack of chest pain on admission (2.3 vs. 1.7). Delays were also longer with transfer from another hospital (3.3 vs. 1.8), with non-daytime presentation (2.0 vs. 1.7), and in low volume pPTCA hospitals (< 49 per year, 1.9 vs. 1.8). Over six years, there was a disproportionate improvement among patients over 65 years (by 15 minutes), in those without chest pain (by 23 minutes), and among transferred patients (by 47 minutes). **CONCLUSIONS:** Both patient and hospital-related factors delay

pPTCA, and some factors have been addressed to minimize delay. More improvement may be possible, and these results may also lead to a better choice of thrombolysis, pPTCA, or combined strategies in selected patients.

Significant Predictors	N	Delay>2 hr (%)	Comparison Group (%)	Odds Ratio (delay >2 hr)	95% CI
Transferred patients	4692	87	38	10.34	9.39-11.37
No chest pain	2261	61	43	2.05	1.85-2.28
Non-daytime (4pm-8am)	19103	51	38	1.82	1.73-1.90
Lytic contraindicated	5582	60	41	1.48	1.37-1.59
Pre-hospital delay > 2 hr	15699	49	40	1.45	1.39-1.53
Hospital procedures < 49 pPTCA/yr	18371	47	41	1.45	1.38-1.53
Female patients	11784	50	42	1.27	1.21-1.34
Non-white patients	5810	48	43	1.18	1.11-1.26
Age ≥ 65	16631	49	41	1.25	1.18-1.31

POSTER SESSION

1015 Stabile Ischemic Syndrome: Risk Factors and Risk Factor Modification I

Sunday, March 18, 2001, Noon-2:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 1:00 p.m.-2:00 p.m.

1015-75 Increased White Blood Cell Count in Patients With Rapid Angiographic Coronary Artery Disease Progression

Emmanouil G. Zouridakis, Almudena Castro, Raul Schwartzman, Ian D. Cox, Xavier Garcia-Moll, Juan Carlos Kaski. *Cardiological Sciences, St George's Hospital Medical School, London, United Kingdom*

Background. It has been reported that total and differential white blood cell count (WBCC) are prognostic markers in patients (pts) with coronary artery disease (CAD). Disruption of atheromatous plaques with ongoing inflammation has been suggested to play a significant role in rapid CAD progression. WBCC represents an index of systemic inflammatory status. In this study we assessed whether total and/or differential WBCC can predict rapid CAD progression.

Methods. We studied 121 pts (82 men, age: 59±9 ys) with chronic stable angina who were on a waiting list for coronary angioplasty and underwent angiography on 2 occasions. The 1st (diagnostic) angiogram was carried out at study entry and the 2nd 5.2±3.0 months later, immediately prior to angioplasty. Quantitative angiographic analysis was used to assess differences in stenosis diameter between the angiograms. Accepted criteria were used to define CAD progression. WBCC was measured in blood samples taken before the first angiogram.

Results. We assessed 287 lesions with >30% diameter reduction (2.4/patient). CAD progression occurred in 32 (26.4%) pts: 15 (48%) had a >10% diameter reduction of at least one pre-existing stenosis >=50%, 12 (37%) had a >30% diameter reduction of a pre-existing stenosis <50%, 3 (9%) pts developed a new stenosis and 2 (6%) had progression of a lesion to total occlusion. Baseline clinical and angiographic data were similar in pts with and without progression. Total WBCC and neutrophil count were significantly higher in pts with CAD progression than those without [(in: $x10^9$cells/L) 7.8±1.4 vs 6.9±1.5, p=0.001 and 4.7±1.1vs 4.0±1.4, p=0.02 respectively]. Quartile WBCC analysis showed that higher WBCC was associated with an increase in the incidence of rapid CAD progression (p for trends = 0.005). Pts with WBCC count ≥8.3 $x10^9$/L (the median of WBCC distribution) had a 3-fold higher risk for rapid CAD progression (Odds ratio:2.9, 95%CI: 1.2-7.2, p= 0.012). There was no significant difference in lymphocyte or monocyte count between progressors and non-progressors.

Conclusions. Increased WBCC is significantly associated with higher risk for rapid CAD progression. The use of this simple test may help to risk stratify pts with CAD

1015-76 Relationship Between White Blood Cell Count and the Occurrence of Silent Ischemia After Myocardial Infarction

Malgorzata Kurpesa, Ewa Trzos, Maria Krzemińska-Pakula, Zbigniew M. Bednarkiewicz. *Medical Academy, Lodz, Poland*

Background: White blood cell count (WBC)is a sensitive marker of inflammation which may accelerate the progression of coronary artery disease (CAD). Silent ischemia (SI) is known to be at least as prognostically unvafourable as symptomatic one. The aim of the study was to assess the relation between WBC and the occurrence of SI in asymptomatic patients after MI. **Methods:**The study group consisted of 114 pts who had Q-wave MI 3-6 months before.All were clinically asymptomatic. Blood cell count was assessed two times in a week interval and the average WBC was calculated for each patient. The pts were divided into two groups: Group I-48 pts with WBC<7000m3 and Group II-66 pts with WBC>7000ml. Groups were comparable with regard to age, gender, risk factors, localization of MI, left ventricular function, medical treatment.24-hour Holter monitoring was performed in all patients. **Results:**115 silent transient ischemic episodes (TIE)were recorded. 102 TIE(89%)were found in Group II, 13 TIE(11%)in GroupI (p<0,01). All pts in Group II had SI. In Group I SI was recorded in only 9% of pts(p<0,001). The presence of SI in totally asymptomatic postinfarction pts appeared to be strongly correlated with WBC>7000ml. **Conclusions:**1. Silent ischemia is common in postinfarction patients with increased leucocytosis. 2. Postinfarction patients with increased leucocytosis are likely to have more severe CAD even if they are asymptomatic.

1015-101 Plasma Level of Homocysteine Is Inversely Associated With the Development of Collateral Circulation

Yoshitaka Nagai, Hiromi Tasaki, Ryouji Kouzuma, Masato Tsutsui, Masahiro Okazaki, Yasuhide Nakashima. *Univ.Occup.Environ.Health, Kitakyushu, Japan*

[Background] Hyperhomocysteinemia has been established as a new coronary risk factor and is assumed to damage the endothelium, leading to coronary atherosclerosis. However, it is unclear whether hyperhomonocysteinemia can independently reduce the development of collaterals in coronary artery disease (CAD) patients. To investigate the plasma level of homocysteine in relation to the development of collaterals in patients with CAD. [Methods] A series of 105 male patients with angiographically-estimated coronary stenosis were enrolled. The effect of homocysteine levels were analyzed coronary stenosis and collateral circulation. [Results] The plasma level of homocysteine was significantly increased (p = 0.013 by Kruskal-Wallis analysis) in order of control group (n = 23, 9.0 (SD;2.4) micromol/L), single-vessel disease group (n = 49, 11.6 (3.7)micromol/L) and multi-vessel group (n = 33, 12.7 (6.8)micromol/L). Univariate and multivariate analyses in single-vessel group revealed that hyperhomocysteinemia was the negative factor of collateral development (p = 0.0015 and 0.0011, odds ratio 0.69, 95% confidence interval 0.52-0.90). Moreover, the level of homocysteine in poorly-developed collateral group was significantly higher than that in well-developed collateral group in patients with one-vessel disease showing total occlusion (p = 0.034). [Conclusions] This study emphasized that the plasma level of homocysteine is independently- and inversely-associated with the development of collateral circulation in CAD patients.

1015-102 The 5' Flanking Polymorphism in the Heme Oxygenase-1 Gene Is Associated With Coronary Artery Disease Susceptibility in Japanese Patients With Hypercholesterolemia

Hideaki Kaneda, Junichi Taguchi, Tadanori Aizawa, Minoru Ohno. *University of Tokyo, Tokyo, Japan, Cardiovascular Institute, Tokyo, Japan*

Background: Hypercholesterolemia is associated with enhanced oxidative stress due to increased lipid peroxidation leading to atherogenesis. Heme oxygenase (HO) is considered an important defense mechanism to cope with oxidative stress and as an anti-atherogenic mechanism. Previous work has shown that shorter (GT)n repeats in the human HO-1 gene promoter have higher transcription activity in response to oxidative stress than longer repeats. Method and **Results:** We screened allelic frequencies of the (GT)n repeats in the HO-1 gene promoter in 189 patients with known hypercholesterolemia who underwent coronary angiography. Coronary artery disease (CAD) was defined as 75% or more stenosis in one or more of the three coronary arteries. As the distribution of numbers of (GT)n repeats was bimodal, the alleles were divided into two subclasses: shorter (<27 repeats) were class S and longer were class L. Using the chi-square test, a significant association was observed between the genotypes and CAD status (p=0.049). Multivariate logistic regression models revealed that the genotypes were significantly related to CAD status.

Multivariate Regression Models for CAD

Risk factor	Odds ratio (95% CI)	p
Genotype S/S *	0.30 (0.10-0.86)	0.026
Genotype S/L *	0.44 (0.18-1.03)	0.061
Male	2.8 (1.1-6.8)	0.020
Age	1.05** (1.01-1.09)	0.015
Diabetes	2.0 (0.99-4.1)	0.054
Hypertension	0.90 (0.44-1.8)	0.76
Smoker	0.75 (0.33-1.7)	0.48
HDL-cholesterol	0.97** (0.94-0.99)	0.0048

*: genotype L/L was regarded as a reference point. **: Odds ratio per one-unit increase.
Conclusion: The 5'-flanking polymorphism in the HO-1 gene is associated with CAD susceptibility in Japanese hypercholesterolemic patients. HO-1 may play an important anti-atherogenetic role in hypercholesterolemic patients.

POSTER SESSION

1016 Ultrastructural Observations and Regulation of Apotosis

Sunday, March 18, 2001, Noon-2:00 p.m.
Orange County Convention Center; Hall A4
Presentation Hour: 1:00 p.m.-2:00 p.m.

1016-77 Hypoxia Regulates Connexin 43 Content in Synchronously Contracting Cardiac Myocytes

Mark S. Turner, Guy A. Haywood, W H. Evans, Keith A. Webster, Nanette H. Bishopric. *University of Miami, Miami, FL, Wales Heart Research Institute, Cardiff, United Kingdom*

Background: Ischemia causes uncoupling of cardiac myocytes and has been suggested to reduce the Connexin 43 (Cx43)content and the number of gap junctions. Ischemia, however, is a combination of hypoxia, reduction in glucose, acidosis and buildup of toxic metabolites. We used an established hypoxia model in beating cultured neonatal rat cardiac myocytes to examine the effect of hypoxia on Cx43 levels. Functional gap junctions are responsible for synchronization of beating in this model. **Methods:** Primary cultures of neonatal rat cardiac myocytes were prepared from 1-3 day oid Sprague-Dawley rats. Cells were cultured with 5% fetal calf serum for 4 days and then for 2 days without serum prior to experimentation. All cultures were beating synchronously at 200-300 beats per minute. Cells were exposed to hypoxia (<0.5% oxygen) within a sealed chamber for 8-20 hours. The medium was supplemented with additional glucose and was changed after 8 hours of hypoxia. Hypoxic samples were harvested within the chamber without reoxygenation, and cell proteins were analysed by Western blot using a rabbit polyclonal Cx43 antibody. Blots were subjected to densitometric analysis and results compared using a paired sample Student's t test. **Results:** Cultures continued synchronous beating throughout the experiment. The total Cx43 level increased by 2.06±0.28 (SEM) -fold at 8 hours (p=0.003, n=9) and 1.97±0.21 fold at 20 hours (p<0.001, n=16). Upon reoxygenation Cx43 levels declined slowly, by 26.4% after 4 hours (n=5, p=0.038). **Conclusions:** Hypoxia increases the Cx43 content of cardiac myocytes in culture within 8h; this increase is sustained for a minimum of 20h and is at least partially reversed by reoxygenation. Functional coupling is maintained during hypoxia in the absence of glucose deprivation. Thus, hypoxia alone does not mediate a reduction in gap junction protein content or coupling.

1016-78 Ischemic Preconditioning Prevents Mitochondrial Bcl-2 Depletion and Limits Infarct Size in the Ischemic Rabbit Heart

Tai-Hwang M. Fan, Zhe Jiao, Olena M. Gorodnya, Xi-Ming Yang. *University of South Alabama, Mobile, AL*

Background: We have previously shown that ischemic preconditioning (PC) could suppress cardiomyocyte apoptosis induced by ischemia/ reperfusion. The present study was undertaken to address the question whether Bcl-2, a mitochondrial protein well known for its anti-apoptosis property, plays a role in the cardioprotection of PC. **Methods:** The control group consisted of 6 isolated, perfused rabbit hearts subjected to 30 min of global ischemia followed by 2 h of reperfusion. The PC hearts (n=6) received 5 min of global ischemia followed by 10 min of reperfusion prior to the 30-min ischemia/2-h reperfusion. Infarct size was determined by computer morphometry of TTC stained sections. Mitochondrial Bcl-2 levels were determined by Western blot analysis in a separate series of hearts, in which serial biopsies were taken at baseline and at 5, 10, 20, 30 min of ischemia. **Results:** In this global ischemia/reperfusion model, PC effectively reduced the infarct size by 50% (p<.01 vs control). Mitochondrial Bcl-2 levels were well maintained in the control hearts during the initial 20 min of ischemia, but fell by 40% at 30 min of ischemia (p<.02 vs baseline). In contrast, PC hearts exhibited a 38-41% increase in Bcl-2 levels (p<.05 vs baseline) during the entire 30 min of ischemia. Interestingly, 20 min of global ischemia followed by 2 h of reperfusion resulted in significant contractile dysfunction but produced little evidence of infarction (infarct size 3.3±2.3%, n=6). **Conclusion:** In rabbit hearts, 30 min of ischemia appears to mark the onset of mitochondrial Bcl-2 depletion and myocardial cell death. PC prevents Bcl-2 depletion and significantly limits myocardial cell death induced by 30 min of ischemia. Maintaining mitochondrial Bcl-2 above a critical level may be an important cardioprotective mechanism of PC.

1016-79 Antiapoptotic Effects of Carvedilol Are Not Mediated by Its Beta-Adrenergic Receptor Blocking Properties

Ernst R. Schwarz, Philipp H. Kersting, Dennis Meven, Thorsten Reffelmann, Erik C. Skobel, Peter Hanrath. *Med. Clinic I, RWTH University Hospital, Aachen, Germany, Dept. of Cardiology, Dr. S. Fakeeh Hospital (Harvard Medical International), Jeddah, Saudi Arabia*

Background. Carvedilol is a ß-receptor antagonist with additional a-blocking effects, which is widely used in the treatment of congestive heart failure. The hydroxylated metabolite BM 92.0228 has reduced a-receptor activites and 170-fold weaker beta-blocker properties. We studied the effects of Carvedilol and BM 92.0228 on myocardial infarct size and apoptosis in a rat model of myocardial ischemia and reperfusion. **Methods.** Anesthesized adult Sprague-Dawley rats were subjected to total occlusion of the left coronary artery with subsequent 60 min of reperfusion. Rats were randomized in 6 groups (grp): Grp 1 and 2 received Carvedilol (1mg/kg IV) 5 min prior to 30 min or 60 min of coronary occlusion, respectively, grp 3 and 4 received BM 92.0228 (1mg/kg IV) prior to 30 or 60 min of coronary occlusion, respectively, and grp 5 and 6 received vehicle prior to 30 or 60 min of coronary occlusion, respectively. After excision of the hearts, ischemic areas of risk were determined by use of blue dye, infarct sizes were planimetrically determined by use of triphenyltetrazolium chloride staining, and expressed as % of risk areas. Myocardial tissue was obtained from the margin zones of the ischemic (non-infarcted) areas for using the TUNEL-method (in situ visualization of apoptotic myocytes by direct anti-digoxigenin detection and expressed as the number of apoptotic cells/total number of cardiomyocytes x 100 = apoptosis index (ApX)). **Results.** Risk areas were similar among the grp (n=6 per grp). Infarct size/risk area was 9±8% in grp 1, 37±13% in grp 2 (p<0.05), 27±12% in grp 3 (p<0.05 vs. grp 1), 42±12% in grp 4 (p<0.05 vs. grp 1 + 3), 31±13% in grp 5(p<0.005 vs. grp 1 + 3), and 48±13% in grp 6. ApX was 5±1% in grp 1, in grp 2 12±2%, in grp 3 7±1%, in grp 4 13±2%, and significantly smaller compared to controls (in grp 5 17±3%, p<0.05, in grp 6 26±1%, p<0.001). **Conclusion.** Carvedilol as well as its metabolite BM 92.0228 reduced infarct size in a 30 min coronary occlusion model, whereas prolonged ischemia eliminates infarct-limiting effects. We hypothesize that the cardioprotective effects of Carvedilol are independent on its ß-blocking properties, but might be mediated by potential antioxidant and direct anti-apoptotic effects.

1016-80 Induction of Pro-Apoptotic Bcl-Xs Protein Expression During Myocardial Infarction but Not After Stunning

Bysani Chandrasekar, Gregory L. Freeman. *University of Texas Health Science Center, San Antonio, TX*

Background: Inhibition of NF-kappaB activation induces apoptosis in a highly cell- and stimulus-specific manner. The goals of this study were (1) to determine whether stunning induces apoptosis, (2) whether inhibition of NF-kB activation during stunning promotes apoptosis, and (3) to analyze whether various genes involved in the regulation of apoptosis are differentially expressed during stunning and infarction. **Methods:** 32 male WKY rats were used for the study (4 groups of 8 each). The stunning group underwent 15 min of LAD coronary artery ligation followed by 3 h reperfusion (R). The second group received N-acetyl-L-cysteine (NAC; 600 mg/kg, i.p.) 1 h prior to occlusion followed by 3 h R. The infarction group underwent 45 min LAD coronary artery occlusion followed by 3 h R. The sham-operated fourth group served as controls. At the end of 3 h R, tissue from the ischemic zones was separated and frozen for analyses. Expression of pro- (Fas, Fas-L, bcl-Xs, bax) and anti-apoptotic (bcl-XL , bcl-2) genes was analyzed by RNase protection assay, Bcl-XL and Bcl-Xs protein levels by Western blotting, and the extent of apoptosis by TUNEL assay. **Results:** No TUNEL positive cells were detected in either saline- or NAC-treated stunned myocardium. However, cells undergoing apoptosis were readily detected by both TUNEL and by nuclear morphology in infarcted myocardium. Sham-operated animals expressed Fas, bax, bcl-XL and bcl-2 mRNA, but not bcl-X s or Fas-L. Irrespective of duration of ischemia, all six genes were expressed in both stunned and infarcted myocardium. However, significantly higher pro-apoptotic (Vs. stunned; bcl-Xs [1.53-fold, p<0.001], Fas-L [1.31-fold, p<0.05], bax [1.26-fold, p<0.05]) and lower anti-apoptotic (bcl-2 [1.15-fold, p<0.05]) gene expression was detected in infarcted myocardium. Most importantly, the pro-apoptotic Bcl-Xs protein was only detected in infarcted myocardium. **Conclusions:** Inhibition of NF-k B activation does not induce apoptosis during stunning. The balance between pro- and anti-apoptotic genes is critical in inducing apoptosis, and longer durations of ischemia drive this balance towards pro-apoptotic gene expression resulting in cell death.

1016-81 Calcineurin Inhibition With Cyclosporin A Preserves Heart Function by Decreasing Apoptosis

Lieven Pool, Thomas N. Masters, Alexander Fokin, Miroslav Barancik, Tibor Ziegelhoeffer, Francis Robicsek, Jutta Schaper. *Max-Planck-Institute, Bad Nauheim, Germany, Heineman Medical Research Center, Charlotte, NC*

Background: Recently, we showed that the addition of cyclosporine A (CsA) to the University of Wisconsin (UW) solution increased functional recovery from 55 to 100% after 18 hours of hypothermic global ischemia in the working heterotopic heart transplant model. Since CsA is known to maintain mitochondrial permeability pores thereby inhibiting apoptosis and to inhibit calcineurin, we determined the rate of apoptosis, the total amount of calcineurin and its degree of activation in this ischemia model.

Methods: Twelve dog hearts were preserved for 18 hours (2-4°C) under low perfusion with UW solution (1ml/min). Six hearts were treated with cyclosporine A (10^{-5} mol/l; CsA+) and six served as control (CsA-). Four biopsies of each heart were taken: before transplantation (A), at the end of preservation (B), after 2 (C), and 6 hours (D) of reperfusion.

Western blot analysis for total calcineurin was performed and the activity of calcineurin was determined using radioactively labeled myelin basic proteins and SDS page analysis (both % of control). Lamin B1 staining and TUNEL Method were carried out to detect apoptosis by immunohistochemistry and confocal microscopy (both % of total myocytes). Electron microscopy was used to determine the degree of ischemic injury.

Results: Evidence for necrosis was absent, myocytes showed moderate ischemic injury that rapidly recovered after reperfusion. ATP was moderately decreased in CsA- but well preserved in CsA+ animals. Further results see table.

Conclusions: CsA inhibits apoptosis probably by 2 different mechanisms: It maintains the integrity of the mitochondrial permeability pore thereby preventing loss of bcl2 and release of cytochrome C, and it prevents stimulation of the proapoptotic factor BAD by inhibition of calcineurin. These effects may be responsible for improved recovery by inhibition of apoptosis in hearts after long ischemic periods which might indicate potential usefulness of CsA in preserving hearts for transplantation.

	A	B	C	D
Apoptotic cells % CsA-/CsA+	0/0	0/0	2.7/1.9	6.0/2.8
Lamin B1 % CsA-/CsA+	99.9/99.5	99.0/99.2	98.1/98.7	92.3/96.9
Calcineurin WB % Csa-/CsA+	100/100	94/98	94/91	63/73
Calcineurin-function CsA-/CsA+	100/100	93/0	-/-	68/0

1016-82 **Cardiac Myofiber Disarray Associated With Postinfarct Remodeling in Viable Border Zones Is Prevented by Treatment With Angiotensin Converting Enzyme (ACE) Inhibitors**

Samuel Wickline, Heather Lewis, Jeffrey Omens, Andrew D. McCulloch, John Allen, Michael Scott, Christopher Hall. *Washington University, St Louis, UCSD, San Diego*

Background: Global cardiac remodeling after infarction implies reorganization of tissue microstructural components that are integrally linked. We sought to elucidate the effects of ACE inhibitors on the specific organization of the interstitial collagen matrix and viable myocytes in infarct, normal, and border zone tissues. **Methods:** Myocardial infarction was induced by left coronary artery occlusion in 12 Sprague-Dawley rats. Ramipril (1 mg/kg/d) was administered in drinking water 3 days after infarction for 12 weeks in 7 rats, and placebo was administered to 5 rats. Picrosirius stained myocardial cross-sections were imaged with circularly polarized light and digitized for collagen analysis; trichrome stains were imaged with light microscopy and digitized for analysis of viable myocytes in border and remote zones. Automated software developed at UCSD was employed for objective quantification of fiber orientation, which was expressed as an Angular standard Deviation (AD: in degrees) with respect to the mean collagen or myocyte orientation in an ROI, to provide an index of microscopic fiber disarray. Five to 10 ROI's each (20X power) were digitized from contiguous midmyocardial locations in remote, border, and infarct zones, and the AD's averaged for each zone over all animals. **Results:** Ramipril decreased relative heart mass by 17% at 12 weeks ($p<0.05$). Ramipril reduced AD for collagen fibers in the border zone from 20.5±2.0 to 14.7± 2.4 degrees; and reduced AD for viable border zone myocytes from 13.8±1.5 to 11.4±1.1 degrees ($p<0.01$ by ANOVA). The AD's in treated border zones approximated those for remote normal tissues for both collagen and myocytes, indicating that ramipril prevented the post infarct disarray of both collagen and myocytes. Ramipril did not affect AD's in either remote normal or central infarct zones. Discussion: ACE inhibitors limit both collagen and myocyte disarray in viable border zones after infarction. These salutary changes in border zone microarchitecture may promote more physiological fiber orientations and strains, potentially improving local contractile function and reducing the stimulus to global ventricular remodeling.

1016-83 **Distinct Signaling Pathways Account for Endothelial and Myocardial Apoptosis During Ischaemia-Reperfusion Injury**

Tiziano M. Scarabelli, Anastasis Stephanou, Carol A. Chen, Terence J. Cooper, Richard A. Knight, David S. Latchman. *University College London, Institute of Child Health, London, United Kingdom, University of Miami, Miami, FL*

The present study was aimed to evaluate the relative contribution of the receptorial and mitochondrial signaling pathways in inducing cardiac apoptosis in different cell types during ischaemia (I)-reperfusion (R) injury. Materials and Methods. Isolated Langendorff perfused rat hearts were randomly divided into 5 groups: control group (60' of perfusion), I group (35' of zero flow I) and 3 I-R groups (35' of I followed by 5', 60' and 120' of R respectively). A few animals were treated with specific and irreversible inhibitors of caspase 8 (C8) and 9 (C9) infused at the onset of I or R. TUNEL staining, propidium iodide and immunocytochemical labeling with anti-Von Willebrand and -desmin antibodies were utilized to assess and address apoptosis in specific cell types. Additional sections were stained with antibodies recognizing the cleaved active form of C8 and C9. Confocal microscopy (CM) analysis was integrated with electron microscopy (EM) observation. Results. Expression of cleaved C8 and C9 was increased both in I and I-R hearts compared to the control group (0.1%), although cleavage of C9 was more pronounced during I (7.7%) whilst C8 was preferentially cleaved during R (6.5% after 60' R). Cleavage of C8 and C9 was confirmed by Western Blotting of frozen samples. The specific inhibitor of C9 given during I dramatically reduced the magnitude of endothelial apoptosis over the 3 time points of R (e.g. 4 versus 44% after 60' R) and only mildly diminished the proportion of TUNEL positive myocytes (e.g. 4.6 versus 6% after 60' R). On the other hand, inhibition of caspase 8 during I consistently prevented myocardial apoptosis measured over R (e.g. 2.2 versus 8.1 after 120' R), without affecting the extent of the process occurring in endothelial cells. Qualitatively identical results were obtained when both inhibitors were infused during R. Immunocytochemical findings were validated by EM. Conclusions. Our data suggest that distinct signaling pathways are induced in different cell types during I-R. Thus, mitochondrial damage is the main trigger of endothelial apoptosis via C9 activation, whilst cardiac myocytes seem to commit apoptosis following death-receptor mediated pathway via C8 activation.

POSTER SESSION

1017 Mechanisms Promising Improved Outcomes With Surgical Revascularization

Sunday, March 18, 2001, Noon-2:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 1:00 p.m.-2:00 p.m.

1017-84 **Myocardial Release of P-Selectin Following Ischemia During Beating Heart Coronary Artery Bypass Surgery**

Tat W. Koh, Simon Davidson, Gerald S. Carr-White, Anthony DeSouza, John R. Pepper. *Royal Brompton Hospital, London, United Kingdom*

Background: Adhesion of leukocytes to the endothelium is mediated by cell adhesion molecules, and has been shown to play a role in myocardial injury during ischemia and reperfusion in animal models. Whether ischemia in the human heart is associated with release of P-selectin is unclear. Beating heart coronary artery surgery requires a period of coronary occlusion to allow grafting in a bloodless field and provides a model of prolonged ischemia in the human heart. **Methods:** We sampled coronary sinus blood draining directly from the heart at the time of coronary artery surgery on the beating heart using the 'Octopus' stabilisation device. We obtained paired arterial blood for calculation of arterio-venous difference and net myocardial release of P-selectin. We studied 16 pts undergoing left anterior descending artery grafting: pre coronary occlusion, and 1 & 5 mins after reperfusion. We analysed the samples for soluble P-selectin and troponin I, a specific marker of myocardial injury. Coronary artery occlusion time was 17.2±5.6 mins. **Results:** P-selectin levels increased in the coronary sinus blood at 5 mins after reperfusion vs pre (44.9±9.1 vs 37.6±4.2 ng/mL, $P<0.05$). Arterial P-selectin levels did not change at 1 and 5 minutes vs pre (42.6±7.9, 37.9±6.0 vs 44.9±6.4 ng/ml). Arterio-venous difference at 5 minutes showed net myocardial release of P-selectin vs pre (-11.5±5.9 vs 5.85±3.8 ng/ml, $P<0.001$). Troponin I levels in coronary sinus blood were elevated after 5 minutes reperfusion vs pre (0.12±0.03 vs 0.05±0.01 mg/l, $P<0.05$). Coronary sinus P-selectin correlated closely with troponin I levels at 5 minutes ($r=0.64$, $P<0.005$). **Conclusion:** Myocardial release of P-selectin occurs after ischemia induced by 17 minutes of coronary occlusion during beating heart coronary artery surgery. Coronary sinus P-selectin levels correlated with the degree of myocardial injury assessed by troponin I. Since leukocyte adhesion may play a role in ischemia-reperfusion injury, therapeutic measures aimed at interfering with the leukocyte-endothelial interaction mediated by cell adhesion molecules, may be a rational target for myocardial protection strategies in beating heart coronary artery surgery.

1017-85 **Coronary Bypass Surgery in Women: A 25 Year Comparative Study of the Impact of the Internal Mammary Artery on Short and Long Term Results in Men and Women**

Paul Kurlansky, Ernest A. Traad, David L. Galbut, Melinda Zucker, George Ebra. *Miami Heart Research Institute, Miami Beach, FL*

Background: Coronary artery bypass grafting (CABG) carries a higher operative mortality and less favorable long-term clinical benefit for women than it does for men. Although arterial revascularization has been shown to ameliorate the impact of gender on operative mortality, its impact on long-term prognosis has not been clearly defined. **Methods:** A retrospective analysis was performed comparing 261 consecutive women patients from a single surgical practice receiving bilateral internal mammary artery (BIMA) and supplemental vein grafts between January 1972 and October 1994 with a computer-matched cohort of 261 men undergoing BIMA surgery during the same time period. Follow-up was complete for 97.6% of women and 96.8% of men, and ranged from 1 month to 25 years, with a mean follow-up of 9.1 years for women and 8.6 years for men. **Results:** There was no significant difference in operative mortality, nor in the incidence of any post-operative complications. Univariate analysis of preoperative and intraoperative variables revealed the same three factors significantly associated with hospital mortality in men and women: Canadian Classification System (CCS) Class IV angina, history of previous CABG, and preoperative insertion of the intra-aortic balloon pump. The actuarial survival at 15 years was 53.7%±4.8% for women and 50.9%±5.6% for men ($p=0.21$). At follow-up, 97% of women and 96% of men were in CCS Class I. The need for reoperation (1.8% vs. 1.9%) and PTCA (4.8% vs. 3.2%) was comparable in both groups. Rate of non-fatal MI was 1.8% in women and 0.6% in men. Cox regression analysis of significant univariate preoperative, intraoperative and postoperative variables demonstrated that a history of congestive heart failure ($p<0.001$) was the most powerful predictor of late mortality in both women and men. Other significant variables included low cardiac output ($p<0.001$) in women and surgical urgency ($p<0.004$) in men. **Conclusions:** Matched groups of men and women undergoing BIMA grafting experience comparable perioperative outcomes and excellent long-term results. The use of the internal mammary artery in these patients seems to eliminate the influence of gender on short and long term results.

1017-86 **Pressure-Flow Relationship in Coronary Bypass Grafts Early After Myocardial Revascularisation**

Beat H. Walpoth, Dirk Springe, Beat Kipfer, Pascal Berdat, Peter Neidhart, Otto M. Hess, Thierry Carrel. *Swiss Cardiovascular Center, Bern, Switzerland*

Background: Coronary bypass flow is dependent on the qualitiy of the anastomosis, perfusion pressure and distal coronary vascular resistance. The aim of the present study was to assess pressure-flow relations in arterial and venous bypass grafts. **Methods:** 30

patients (28 M; 2 F; 62 ± 8 yrs) underwent elective coronary bypass grafting (3.5±1.0 grafts/patient) under mild hypothermic cardiopulmonary bypass (CPB) (77±24 min.). After weaning from CPB, coronary bypass flow was measured on one arterial (IMA) and one venous (SVG) bypass graft using the transit time technique (CardioMed, MediStim AS, Norway). Mean arterial pressure (MAP) was modified gradually by the infusion of norepinephrine (maximum cumulative dose = 13 ug) and/or nitroglycerin (maximum cumulative dose = 412 ug) in order to increase respectively decrease MAP by at least 10%. **Results:**

Variable	Baseline	Norepinephrine	Nitroglycerin	p
MAP (mmHg)	75 ± 9	94 ± 11	59 ± 9	<0.05
IMA flow (ml/min)	37 ± 17	43 ± 20	27 ± 12	<0.02
SVG flow (ml/min)	67 ± 37	74 ± 46	57 ± 34	ns

With the maximum norepinephrine or nitroglycerin dose respectively, MAP increased by 25% or decreased by 21%, IMA graft flow increased by 16% and decreased by 27% (p<0.001) and SVG flow increased by 10% and decreased by 15% (p<0.01) respectively. Resistance changes were not significant for both IMA and SVG grafts. There was a significant pressure-flow relationship with a correlation coefficient of r = 0.6 for IMA and r = 0.5 for SVG grafts, respectively. **Conclusions:** There is a linear pressure-flow relationship for arterial and venous bypass grafts early after revascularization. Coronary vascular resistance remains, however, unchanged suggesting that pressure-flow relationship is maintained even after pharmacologic manipulation. Thus, adequate perfusion pressure is mandatory after myocardial revascularisation, especially for IMA grafts.

1017-87 Indomethacin in OPCAB Reduces Postoperative AFIB

Allison J. McLarty, Edward Woodford, Frank Seifert, Thomas V. Bilfinger, Adam E. Saltman, Irvin B. Krukenkamp. *State University of New York at Stony Brook, Stony Brook, NY*

Background: Post-operative atrial fibrillation (AFIB) is a common complication following CABG. Previous reports have not shown an impact of off pump CABG (OPCAB) on the incidence of AFIB. **Methods:** We reviewed our experience with CABG over a 12 month period to assess the impact of OPCAB on post-operative AFIB in our institution. From 7/1/98 to 6/30/99 750 patients underwent CABG only. **Results:** 379 operations were performed with extracorporeal circulation (ECC) and 371 were without (OPCAB). There was no significant difference between the groups in the mean age of the patient (64+/-SD11 vs. 63+/-12 years), sex (76 vs. 69% men), ejection fraction (45+/-SD12 vs. 47+/-SD13), number of grafts (3.7+/-SD2 vs. 3.1+/-SD1), preoperative AFIB (5%), preoperative treatment with beta blockers (51 vs. 48%) or calcium-channel blockers (32 vs. 27%) or length of stay (5+/-SD2 days). Post-operative prophylaxis against AFIB with beta-blockers was also comparable between the groups (85 vs. 74%). One surgeon in the group added the non-steroidal anti-inflammatory drug (NSAID) Indomethacin to the medical regimen of his OPCAB patients to treat the observed increased incidence of post-pericardiotomy syndrome. The incidence of AFIB in the entire group was decreased from 26% in patients undergoing CABG with ECC to 18% in those with OPCAB (p=0.013). There was no difference in the severity of AFIB between the groups with 63% of patients with ECC experiencing shortlived AFIB (<48 hours)vs. 71% of OPCAB patients. Importantly, in OPCAB patients on Indomethacin, the incidence of AFIB was only 7% compared to 20% in those not on Indomethacin (p=0.039). Comparing OPCAB patients not on the NSAID to CABG patients with ECC, the rate of AFIB was seen to be the same. **Conclusion:** We conclude that OPCAB does not decrease the incidence of postoperative AFIB. However, the addition of the NSAID Indomethacin resulted in a significant decrease in this arrythmia. A prospective randomized trial of the post-operative use of this agent in patients undergoing CABG is warranted.

1017-88 Effect of Early Postoperative Shear Stress on Late Postoperative Remodeling of Aortocoronary Bypass Graft

Hiroshi Sato, Masao Okamura, Takeyoshi Ohta, Keiji Kurogane, Ryouhei Kuroda, Takashi Kajiura. *Takatsuki General Hospital, Takatsuki-city, Japan*

Although experimental studies have showed that intimal hyperplasia of bypass graft is regulated in response to changes in shear stress (SS), little is known about remodeling in aortocoronary bypass. The purpose of this study is to explore the effect of early postoperative SS on late postoperative remodeling in bypass graft and clinical outcome. (Methods) Thirty five SVGs and 13 LITA were studied at both 1 month and 2 years after surgery in each graft. Average peak velocity (APV) by Doppler guidewire and graft diameter (D) by quantitative angiography were measured. SS was calculated by these parameters (SS = 80 x 0.035 x APV / D dyn/cm2). Thirteen LITA were defined as Group A and 35 SVGs were divided into two groups according to early postoperative SS: Group H (n=19) SS>10 dyn/cm2, Group L (n=16) SS<10 dyn/cm2. Normal value of SS in proximal coronary artery was 16.4+/-7.9 dyn/cm2 in our laboratory.(Results) Group A indicated higher SS than normal value early after surgery, which decreased significantly with enlargement of D late postoperatively (SS: 30.8+/-9.7 to 23.9+/-6.6 dyn/cm2, p<0.05, D: 1.9+/-0.3 to 2.2+/-0.4 mm, p<0.05) with excellent patency (100%). Group H showed normal SS early after operation, which did not change significantly late after operation with less reduction of D (SS: 17.0+/-6.0 to 15.6+/-6.8 dyn/cm2, n.s., D: 3.5+/-0.5 to 3.1+/-0.6 mm, p<0.001) than Group L, and indicating excellent patency (100%). SS in Group L was significantly lower than normal value early after surgery, which increased late postoperatively with excessive reduction of D (SS: 5.6+/-1.9 to 8.7+/-4.1dyn/cm2, p<0.01, D: 4.5+/-1.2 to 3.7+/-1.3 mm, p<0.0001). Clinically three out of 16 grafts in Group L were occluded. (Conclusions) LITA showed enlargement of D to regulate its SS late postoperatively. SVGs with lower SS early after surgery showed excessive reduction of D late postoperatively, which would be due to excessive intimal hyperplasia. Even in two years follow up periods, graft failures were noted in this group. On the other hand, SVGs with normal SS early after surgery showed little remodeling late postoperatively with better graft patency.

POSTER SESSION

1018 Myocardial Pathogenetic Aspects in Acute Coronary Syndromes

Sunday, March 18, 2001, Noon-2:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 1:00 p.m.-2:00 p.m.

1018-89 The New Definition of Myocardial Infarction: What Does It Mean Clinically?

Mark A. Meier, Wisam H. Al-Badr, Jeanna V. Cooper, Eva M. Kline-Rogers, Kim A. Eagle, Raj H. Mehta. *University of Michigan, Ann Arbor, MI*

Background: The diagnostic criteria for myocardial infarction are being revised to include either troponin (I or T) or CKMB in addition to symptomatology and ECG changes. However, the clinical significance of using these new criteria is unknown.
Methods: All patients admitted to the University of Michigan Medical Center from May 1, 1999 to January 1, 2000 with a suspected acute coronary syndrome(ACS) were entered into the ACS Database. Baseline demographics and in-hospital measures were obtained by chart review. By phone call and chart review, a 6 month follow-up was performed. Patients were stratified according to peak CKMB and troponin I and compared using chi-squared analysis.
Results: Among patients who had both troponin I and CKMB measured, 305 patients with enzyme elevations were identified and separated into two groups. Group A contained patients with an elevated CKMB regardless of troponin status and Group B contained patients with an elevated troponin I and normal CKMB. Group A patients were significantly younger and required more percutaneous coronary interventions. Although not statistically significant, patients in Group B tended to have a shorter hospital stay and fewer in-hospital events including shock, need for bypass, death, and reinfarction. In addition, patients in Group B tended to have a lower 6 month mortality.
Conclusion: The decision to include troponin in the diagnostic criteria will result in a 16% increase in the annual number of myocardial infarctions diagnosed at our institution, and may select a clinically less complicated patient population. The implications, both clinical and financial, are far-reaching.

Demographic, In-hospital, and Follow-up Data

	Group A (+CK)	%	Group B (-CK+TnI)	%	p-value
Total n	264		41		
Male	177	67.0	21	51.2	0.048
Age	64.1 +/- 13.9		68.8 +/- 11.6		0.043
In-hospital Events					
CHF	28	10.6	5	12.2	ns
Shock	25	9.5	2	4.9	ns
PTCA/Stent	144	54.8	9	22.0	<0.001
CABG	16	6.2	1	2.4	ns
Death	18	6.8	1	2.4	ns
Nonfatal MI	13	4.9	1	2.4	ns
Length of stay	5.8 +/- 7.1		4.5 +/- 3.9		ns
Follow-up					
Death at 6 months	18	8.5	2	5.4	ns

1018-90 Prediction of the Site of Myocardial Infarction Using Exercise Echocardiography

Helen L. Thomson, Abdou Elhendy, Douglas W. Mahoney, Patricia A. Pellikka. *Mayo Clinic and Foundation, Rochester, MN*

Introduction: Stress echocardiography can predict the occurrence of myocardial infarction (MI) and cardiac death. In this study we investigated if stress echocardiography could predict the site of MI
Method: We identified a cohort of 128 patients (94 male, 34 female, mean age 65±10) who had stress echocardiography between 1990 and 1995 and subsequently had a MI. Exclusion criteria included coronary revascularization between the stress echocardiography and the MI. Exercise echocardiography was performed in according to our usual protocol and the location of wall motion abnormalities at rest and with stress was determined. The site of the MI was localized using post MI ECG, echocardiogram, and/or review of the history.The MI was classified as anterior, inferior, antero-lateral or postero-lateral. The association of ischemia or fixed abnormality in a specific territory with the occurrence of MI in the corresponding territory was investigated using the Chi-square test or Fisher's Exact Test where appropriate. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of an ischemic finding to predict site of MI were assessed in a standard fashion
Results: The median time from the exercise echocardiogram to occurrence of MI was 2.1 years (range: 1 day-7 years). There was no significant association of ischemic findings or ischemic+ fixed abnormalities in the anterior (p=0.16 & p=0.40), inferior (p=0.46 & p=0.30), anterolateral (p=0.48 & p=0.62), or posterolateral (p=0.62 & p=0.99) territories with the corresponding territory of MI involvement, respectively.

Territory Involved*	N	Sensitivity(%)	Specificity(%)	PPV (%)	NPV
Anterior	53	34 (53)	77 (55)	51 (45)	62(62)
Inferior	58	36 (72)	70 (37)	50 (49)	57 (62)

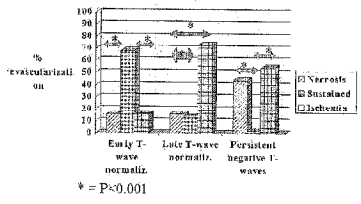
Anterolat	6	17 (33)	90 (78)	8 (7)	96 (96)
Posterolat	11	18 (36)	89 (66)	13 (9)	92 (92)

*Statistics for fixed+ischemic abnormalities are within parentheses.

Conclusion: Stress echocardiography had previously been demonstrated to provide incremental and independent prognostic information to the risk of subsequent MI. However the resultsof this study suggest the ability of stress echocardiography to predict the actual site of subsequent MI is limited.

1018-91 Determinants of Persistent Negative T Waves and Early Versus Late T Wave Normalization After Acute Myocardial Infarction

Luc A. Pierard, Patrizio Lancellotti, Paul L. Gerard, Ali R. Bilge, Henri E. Kulbertus. *University hospital of Liege, Liege, Belgium*



Background: The clinical significance of T wave normalization vs persistent negative T waves in the infarct related leads after AMI remains controversial. **Methods:** 127 consecutive pts with first AMI and >2 negative T waves in infarct related leads on 24-hour ECG underwent dobutamine-atropine stress echocardiography(DSE) 4±2 days after AMI. Coronary angiography was available in all and elective angioplasty of infarct related artery was performed in 77. 12 lead ECG was recorded at hospital discharge(early) and at 4±1 months(late) **Results:** T-wave normalization was observed in 88 pts(early in 19 and late in 69) DSE showed sustained improvement in 23, ischemia in 73(51 biphasic response and 22 ischemia in adjacent area) and unchanged akinesia in 31. Fig represents the repartition of DSE responses in the 3 ECG subgroups. **Conclusions:** 1. Early T normalization is associated with sustained improvement suggesting stunning myocardium 2. Late normalization is mainly observed in pts with ischemic myocardium frequently revascularized. 3. Persistent negative T-waves correspond to either transmural necrosis or non revascularized hibernating myocardium.

1018-92 Is Initial Antegrade Flow Same to Early Reperfusion in Patients With Acute Myocardial Infarction?

Masaharu Ishihara, Hikaru Sato, Takuji Kawagoe, Yuji Shimatani, Satoshi Kurisu, Kenji Nishioka, Yasuyuki Kouno, Takashi Umemura, Shuji Nakamura. *Hiroshima City Hospital, Hiroshima, Japan*

Background: Antegrade flow before coronary angioplasty has shown to be associated with favorable outcome after acute myocardial infarction, justifing antecedent intravenous thrombolysis before angioplasty. However, it remains unknown whether spontaneous initial antegrade flow is same to antegrade flow achieved by early reperfusion therapy. **Methods:** This study consisted of 450 consecutive patients with a first anterior wall acute myocardial infarction in whom coronary angiography was performed within 12 hours after the onset chest pain and TIMI grade 3 flow was obtained after reperfusion therapy. They were divided into 3 groups: 149 patients with initial antegrade (TIMI grade 1-3) flow (group 1), 58 patients with initial TIMI grade 0 flow and time to reperfusion <2 hours (group 2) and 243 patients with initial TIMI grade 0 flow and time to reperfusion ≥2 hours (group 3). **Results:** In-hospital mortality was 0.7% in group 1, 3.5% in group 2 and 5.4% in group 3 (p=0.03). Acute left ventricular ojection fraction was significantly better in group 1 (54±13%) than group 2 and group 3 (47±10% and 47±10%, respectively; p<0.001). Predischarge left ventricular ejection fraction was 64±15% in group 1, 55±13% in group 2 and 51±14% in group 3 (p<0.001). Transient chest pain episode(s) within 24 hours before infarction was more frequent in group 1 (42%) than group 2 and group 3 (33% and 31%, respectively; p=0.03). **Conclusion:** Although early reperfusion was associated with favorable outcome, initial antegrade flow had more impact than early reperfusion of initially occluded infarct artery. Our results suggest that pathogenesis of initial antegrade flow might be different from that of early reperfusion, i.e., intermittent occlusion.

1018-93 Increased QT Dispersion in Patients With Prinzmetal's Variant Angina and Cardiac Arrest

Nikhil Parchure, Juan C. Kaski. *Cardiological Sciences, St George's Hospital Medical School, London, United Kingdom*

Objectives. We sought to compare QT dispersion in patients presenting with Prinzmetal's variant angina complicated by cardiac arrest or syncope and patients with uncomplicated variant angina.

Background. Despite the usually benign course of treated Prinzmetal's variant angina, a proportion of vasospastic angina patients develop ventricular arrhythmias and sudden death in association with coronary spasm. Increased QT dispersion has been suggested to increase susceptibility to ventricular arrhythmias in patients with coronary artery spasm.

Methods. We studied 25 consecutive patients (mean age 58 years; 14 men) with classical Prinzmetal's variant angina and documented coronary artery spasm. None of the patients had coronary artery stenoses ≥40%. Five patients had suffered a documented cardiac arrest, 2 had recurrent syncope and 18 had no arrhythmic events or syncopal episodes. In all patients clinical and biochemical variables were measured at study entry. QT dispersion (QT maximum – QT minimum in every ECG lead) was measured on the baseline 12-lead electrocardiogram at study entry using a digitising board.

Results. No significant clinical, biochemical or angiographic differences were found between patients with and those without cardiac arrest or syncope. Mean (± SD) QT dispersion of the whole group was 62.3 ± 19.5 ms. QT dispersion was significantly higher in patients with cardiac arrest or syncope (79.4 ± 17.3 ms) compared to patients with no such events (56.3 ± 16.9 ms), (95% CI 7.5-38.8, P=0.005).

Conclusion. QT dispersion is increased in patients with Prinzmetal's variant angina complicated by cardiac arrest and syncope compared to patients without such events. Increased QT dispersion may be both a substrate for sudden cardiac death and a marker of risk in patients with Prinzmetal's variant angina.

1018-94 Acute Myocardial Infarction in Patients With High Lp(a) Levels Is Highly Characterized by Absence of Prodromal Angina and Early Culprit Artery Patency and Presence of Cardiac Dysfunction

Tatsuaki Murakami, Ikuo Moriuchi, Sumio Mizuno. *Fukui Cardiovascular Center, Fukui, Japan*

Background; Although Lp(a) has been recognized as a related factor to coronary artery disease, clinical impacts of high Lp(a) levels on acute myocardial infarction (AMI) remained uncertain in the era of aggressive recanalization strategy. This study investigated characteristics of AMI in patients with high Lp(a) levels. **Methods;** We evaluated clinical and angiographic variables in the consecutive AMI patients (n=250) who underwent emergent CAG, and compared the variables in patients with high Lp(a) levels (Lp(a); 30mg/dl or more, Group-L) to those in patients with normal Lp(a) levels (Group-C). **Results;** There were no significant differences in other coronary risk factors, location of myocardial infarction, culprit artery, number of stenosed vessels, or collateral supply. Patients of Group-L (n=60) manifested less frequent prodromal angina (PAP), and more frequent cardiac dysfunction defined by abnormal Killip or Forrester class. Patients of Group-L had larger elevation of creatine phosphokinase (CK). Incidence of early patency (TIMI flow grade 3) was low. Left ventricular enddiastolic pressure (LVEDP) was higher. Left ventricular ejection fraction (LVEF) was lower. The differences about cardiac dysfunction remained significant in subgroup absent from PAP or TIMI flow grade 3. **Conclusion;** These results indicate that AMI patients with high Lp(a) levels are highly characterized by absence of prodromal angina and early culprit artery patency and presence of cardiac dysfunction, which may be of great clinical implication on managemnet of myocardial infarction.

Clinical and Angiographic Variables in 2 Groups

	Group-L	Group-C	p value
PAP	11(18%)	62(32%)	0.039
Cardiac Dysfunction	17(28%)	21(11%)	0.002
CK	3904±2870	2235±1901	<0.001
TIMI-3	6(10%)	47(25%)	0.016
LVEDP	22±6	18±6	<0.001
LVEF	50±15	59±13	<0.001

POSTER SESSION

1019 Novel Pharmacological Treatments for Acute Myocardial Infarction

Sunday, March 18, 2001, Noon-2:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 1:00 p.m.-2:00 p.m.

1019-95 Impact of Intravenous Nicorandil on Coronary Microvascular Function in Patients With Acute Myocardial Infarction: Study With Doppler Guidewire

Koichi Yamamoto, Hiroshi Ito, Katsuomi Iwakura, Yasunori Shintani, Akinobu Katoh, Masashi Ikushima, Shigeo Kawano, Yorihiko Higashino, Kenshi Fujii. *Division of Cardiology,Sakurabashi Watanabe Hospital, Osaka, Japan*

We previously reported that intravenous nicorandil (NIC), hybrid of nitrates and K_{ATP} channel opener, improves myocardial perfusion and provides better clinical outcomes in patients with anterior AMI. The goal of this study was to assess whether this beneficial effect is related solely to the improvement in coronary microvascular function or not. We divided 73 patients with AMI, who underwent PTCA/STENT, into 2 groups: with (NC, n=35) and without (C, n=38) intravenous NIC. In NIC, we injected 6 mg of NIC after the diagnosis of AMI, followed by intravenous injection of 6 mg/h for 24 hours. In each patient, we recorded coronary blood flow velocity with Doppler wire and measured diastolic deceleration time (DDT, msec) as an estimate of microvascular function. We performed 2-D echo at days-1 and 21 and calculated wall motion score index (WMSI, average of segment scores (normal=0 to dys/akinesis=3) within the infarct zone). **Results.** There was no WMSI at day-1 between 2 groups. DDT and •WMSI(1d-21d) were significantly higher in NC than in C (NC vs. C; 410 vs. 340 and 1.1 vs. 0.6, p<0.01). The regression line between DDT and •WMSI (1d-21d) in NC is placed upper left of that in C. Multiple regression analysis documented that distributions of plots were significantly different between two groups. **Conclusion.** Beneficial effect of intravenous

NC was partially explained by the improvement in microvascular function (an increase in DDT). But its direct impact of NIC on myocardial protection is speculated since •WMSI(1d-21d) is greater than that expected from DDT value in C.

1019-96 Elevated C-Reactive Protein Levels on Admission Are Related to ST Segment Elevation Resolution in Patients With Acute Myocardial Infarction

Michael Zairis, Stavros Manousakis, Alexander Stefanidis, Denis Vitalis, George Andrikopoulos, Stelios Handanis, Kostas Katsaros, John Hadjissavas, Spyros Argyrakis, Panayiotis Asimakopoulos, Stefanos Foussas. *Cardiology Department, Tzanio Hospital, Piraeus, Greece*

Background: Failure of ST segment resolution after thrombolysis for acute myocardial infarction defines a high-risk group of patients. Additionally, high levels of plasma C-reactive protein assayed in the first few days after acute myocardial infarction have been associated with an unfavorable outcome. However, the possible association of plasma C-reactive protein levels with the outcome of thrombolytic therapy has not been clarified yet. The aim of this study was to evaluate the possible association of plasma levels of C-reactive protein to ST segment resolution after thrombolysis for acute myocardial infarction. Methods and **Results:** A total of 214 patients presenting <=6 hours from onset of acute myocardial infarction were studied. ST segment elevation was measured upon admission and two hours after the commencement of thrombolytic therapy. High plasma levels of C-reactive protein on admission was found to be an independent adverse predictor of, the probability of complete ST segment resolution (>=70% resolution of the initial sum of ST segment elevation) achievement (b=-0.46, RR=0.63, 95%CI=0.48-0.82, p=0.001) 2 hours after administration of thrombolysis. **Conclusions:** Plasma levels of C-reactive protein in the first six hours of acute myocardial infarction can predict the extent of myocardial reperfusion due to fybrinolytic therapy. Thus, plasma C–reactive protein levels on hospital admission may serve as an affordable and widely available marker for the detection of patients with myocardial reperfusion failure. These patients could benefit from more aggressive pharmaceutical or invasive treatment.

1019-97 Effects of Angiotensin II Receptor Blockade on Fibrinolysis and Coagulation in Patients With Acute Myocardial Infarction

Hirofumi Soejima, Hisao Ogawa, Keiji Takazoe, Shinzo Miyamoto, Ichiro Kajiwara, Hideki Shimomura. *Department of Cardiovascular Medicine, Kumamoto University School of Medicine, Kumamoto City, Japan*

Background. It has been reported that angiotensin II type 1 (AT1) receptor antagonism is associated with an improvement in mortality in patients with symptomatic heart failure. We investigated the effects of AT1 receptor antagonist on plasma plasminogen activator inhibitor (PAI), tissue type plasminogen activator (t-PA), and tissue factor (TF) levels in patients with acute myocardial infarction. **Methods and Results.** In a randomized, double-blind, placebo-controlled study beginning one week after acute myocardial infarction, 14 patients received 4 weeks of losartan 25 mg daily therapy (losartan group) another 14 received enalapril 5 mg daily therapy (enalapril group), and the other 14 received placebo (placebo group). We performed blood sampling on the day before the start of administration, and on the day 3, 7 and 28 after the start of administration. There were no significant differences in the plasma PAI, t-PA, or TF levels before the administration among the three groups. The plasma PAI activity and TF antigen levels significantly decreased by the day 28 in the losartan and enalapril groups. These two variables were unchanged during the study period in the placebo group. The plasma PAI activity and TF antigen levels on day 28 in the losartan and enalapril groups were significantly lower than that in the placebo group. There were no difference in the decrease in plasma PAI activity and TF antigen levels after administration between the losartan and enalapril groups. (The plasma PAI activity (IU/mL) losartan and enalapril and placebo :11.7 and 11.4 and 12.0 before the administration, 6.7 and 6.7 and 12.7 on day 28) (The plasma TF antigen levels (pg/mL) losartan and enalapril and placebo : 231 and 229 and 237 before the administration, 184 and 176 and 245 on day 28) T-PA antigen levels did not change in these three groups. **Conclusions.** This study demonstrated that AT1 receptor antagonism as well as angiotensin converting enzyme (ACE) inhibition improves impared fibrinolysis and hypercoagulability in patients with acute myocardial infarction. It may be an evidence that administration of AT1 receptor antagonist as well as ACE inhibitor is effective therapy for the patients with acute myocardial infarction.

1019-98 Complement Inhibition and Myocardial Protection in Patients With Acute Myocardial Infarction

Chris de Zwaan, Appie Kleine, Jard Diris, Jan Glatz, Paul Strengers, Erik Hack, Marja van Dieijen-Visser, Wim Hermens, Hein Wellens. *CARIM University Maastricht, Maastricht, The Netherlands, University Amsterdam, Amsterdam, The Netherlands*

Background: One of the consequences of acute myocardial ischemia is activation of the complement system by various pro-inflammatory cytokines. This process will lead to myocardial cell injury. The C1-esterase inhibitor (C1inh) inhibits the classical pathway of complement activation. We recently studied the effects of C1inh on acute myocardial ischemia in dogs and found that intravenous C1inh, given 2-10 hours after onset of ischemia, diminished myocardial ceil loss in the reperfused as well as the non-reperfused animal heart. This prompted us to study the effects of a continuous infusion of C1inh in patients with acute myocardial infarction after successful thrombolytic therapy. **Methods:** Human C1inh (Cetor), purified from donor plasma, was intravenously administered as a bolus injection, followed by an infusion for 48 hours. Twenty two patients received C1inh. Six hours after the onset of acute myocardial infarction and respectively 1 and 2 hours after the termination of tPA or streptokinase infusion. Effects of C1inh on evolving myocardial injury were estimated from plasma concentrations of the cardiac marker proteins: creatine kinase (CK), MB isoenzyme of creatine kinase mass (CK-MB mass), alpha-hydroxybutyrate dehydrogenase (HBDH) and troponine-T (TnT). Efficacy of complement inhibition was also estimated from the generation of C4 activation fragments. In addition, interleukin-6 and C-reactive protein were measured. **Results:** C1inh resulted in a reduction of 38% (P 0.022), 57% (P 0.001), 18% and 36% of the areas under the - normalized to the 6 hours (pretreatment)- plasma concentration curves of CK, CK-MB mass, HBDH and TnT, respectively, in comparison with 18 matched control patients. A rebound effect or loss of myocardial protection by C1inh 48 and 72 hours after onset of acute myocardial infarction, was not seen. Human C1inh (Cetor) was found to be safe and well tolerated in all patients. **Conclusion:** The reduction of plasma concentration of the cardiac marker proteins CK and CK-MB mass suggests salvage of myocardial tissue, shortening of the time of evolving myocardial necrosis and protection of the cardiac muscle. The beneficial effects of this type of drug warrant further investigation.

1019-99 Nicorandil Improves Functional and Clinical Outcomes in Patients With Acute Myocardial Infarction

Nahoko Ikeda, Takanori Yasu, Norifumi Kubo, Yoshitaka Sugawara, Kazuo Matsushima, Mikihisa Fujii, Muneyasu Saito. *Omiya Medical Center, Jichi Medical School, Omiya, Japan*

Background Recent studies in animals and humans suggested that an adenosine triphosphate sensitive K+ channel (K+ ATP channel) opener exerts cardioprotection after prolonged ischemia. Nicorandil is a hybrid compound of K+ ATP channel opener and donor of nitric oxide (NO). We did randomized prospective study to compare the cardioprotective effect of nicorandil and isosorbideÐdi-nitrate (ISDN) in patients with acute myocardial infarction (AMI). **Methods** Consecutive 60 patients with first episode of AMI within 12 h after the onset were randomly divided into two groups, nicorandil (n=30) and ISDN group (n=30). Each drug was infused intravenously at 3-8 mg/h for 72 h from the admission. All the patients underwent direct balloon angioplasty. Fiftysix patients received successful revascularization and intracoronary administration of ISDN (2mg) or nicorandil (2mg) just after the procedure. Coronary flow velocity and flow reserve also determined by flow wire. Coronary arteriography was repeated in all the patients three weeks after the onset. **Results** There were no differences in baseline clinical characteristics between the two groups. In the nicorandil group, end-systolic volume index and left ventricular ejection fraction after reperfusion were significantly better. The wall motion analysis by centerline method were also better in the nicorandil group (SD/chord: -1.75 vs. -2.66, p<0.05), and those effects lasted to after three weeks (-1.77 vs. Ð2.50, p<0.05). The peak systolic coronary antegrade flow velocity was significantly larger (18.8 cm/s vs. 7.9 cm/s), and the frequency of early systolic retrograde flow, reflecting no reflow phenomenon, was lower in the nicorandil group than in the ISDN group (13% vs. 50%, p<0.05). There were no differences in NO metabolites in blood sampled from coronary sinus between two groups. **Conclusions** Nicorandil can preserve myocardial microcirculation after reperfusion, and leads to improvement of stunned myocardium and decrease of left ventricular remodeling. Those beneficial effects may be associated with K+ ATP channel opener. Therefore nicorandil drip infusion therapy is highly recommended to patients with AMI after successful reperfusion.

1019-100 Hepatocyte Growth Factor: Potential Role of a Novel Vascular Modulator in Acute Myocardial Infarction Patients

Konstantinos I. Kapetanios, Christos E. Pitsavos, Emmanuel V. Economou, Marina G. Toutouza, Christodoulos I. Stefanadis, Pavlos K. Toutouzas. *Hippokration Hospital of Athens, ATHENS, Greece, University of Athens Medical School, ATHENS, Greece*

Background: Hepatocyte growth factor is a member of the endothelium-specific growth factors transducing a wide range of biological signals, acting as an organotrophic factor and exhibiting a potent angiogenic and antiapoptotic activity in several cell types. The aim of our study was to elucidate any possible role of this factor in acute myocardial infarction patients.
Methods: We measured serum hepatocyte growth factor levels in 17 patients with first attack of myocardial infarction, admitted and thrombolysed during the acute phase, and no previous history of any other disease, and compared to those of 17 sex and age-matched healthy controls with mean values: 0,29±0,05 ng/ml. Samples were collected at the time of admission to the hospital and 3,6,9,12,18,24,36,48 hours as well as 3,4,5,7,15 and 30 days thereafter and measured by ELISA method. For the statistical analysis non-parametric Wilcoxon test was used. Data is expressed as mean values ± SEM in ng/ml and considered to be statistically significant with p<0,05 when compared to mean values of healthy controls (*) and the last serum sample (♦).
Results: Hepatocyte growth factor exhibited an initial high level of 7,5±2,9 (*♦), reaching a peak of 8,2±2,9 (*♦), 3 hours after admission, followed by a gradual decrease, reaching a minimum level of 1,9±0,6 (♦) at 36 hours, that was reversed by a rebound up to a maximum level of 5,2±1,8 (*♦) at 3 days . This second peak was also followed by a sustained decline up to a final nadir of 0,3±0,04, at 30 days. Furthermore, patients with extensive acute myocardial infarction and adverse events exhibited a higher, more sustained initial peak compared to those with limited infarct size (16,7±3,8 versus 5,9±1,3, p<0,05).
Conclusion: The initially 27-fold increased hepatocyte growth factor possibly acts as a survival factor against endothelial cell death caused by acute hypoxia due to reduced vascular perfusion, while the following decrease could be attributed to reperfusion due to thrombolytic therapy. Raised levels of this factor, 3 days later, may be fundamental for the induction of angiogenesis implicated to the process of remodeling, thus preserving cardiac function.

POSTER SESSION

1050 Stabile Ischemic Syndrome: Risk Factors and Risk Factor Modification

Sunday, March 18, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 4:00 p.m.-5:00 p.m.

1050-75 Prognostic Value of Remnant-Like Lipoprotein Particles Levels in Patients With Coronary Artery Disease in Type 2 Diabetes Mellitus

Osamu Honda. *Kumamoto University of Medicine, Kumamoto city, Japan*

Several studies showed that triglyceride (TG)-rich lipoproteins contribute to atherosclerotic complications in type 2 diabetes mellitus (DM). However, it remains undefined which TG-rich lipoproteins contribute to the risk. We have shown that measurement of remnant-like lipoprotein particles (RLP), assessed by an immunoseparation method that is recently developed, is helpful in risk assessment of coronary artery disease (CAD). Thus, this study prospectively examined whether high RLP levels may have a significant risk and prognostic values in type 2 DM patients with CAD. RLP levels in fasting serum were measured in 176 consecutive type 2 DM patients with (n=87) or without (n=89) CAD by an immunoaffinity gel containing anti-apoA-1 and anti-apoB-100 monoclonal antibodies. The patients with CAD were followed up for ≤24 months until occurrence of the following clinical coronary events; readmission or coronary revascularization due to recurrent or refractory angina pectoris, nonfatal myocardial infarction, and cardiac death. Patients with CAD had higher RLP levels than those without CAD (7.2±1.0 mg cholesterol/dl vs. 4.2 0.5 mg/dL, P=0.001). Multivariate logistic regression analysis showed that high RLP levels (>4.7 mg cholesterol/dL; 75th percentile of the distribution of RLP levels in controls) were a significant risk factor for the presence of CAD independent of age (>70 y), sex (male), smoking, hypertension, hypercholesterolemia, high LDL levels, low HDL levels, and hypertriglyceridemia (Odds ratio;1.9, 95%CI;1.5-2.2,P<0.01). Kaplan-Meier analysis demonstrated that high RLP levels had higher probability of developing coronary events in patients with CAD (P<0.01). In multivariate Cox hazard analysis, high RLP levels were a significant predictor of developing coronary events independent of other risk factors (Odds ratio;5.5, 95%CI;2.0-15.2, P=0.01). Thus, the increase in remnant lipoproteins levels is a significant risk factor of CAD and predicts future coronary events in type 2 DM patients with CAD independent of other risk factors. Measurement of RLP levels may be useful in assessment of CAD risk in type 2 DM.

1050-76 Circulating Concentration of Cardiac Troponin T Is Useful for Risk Stratification in Patients With Chronic Hemodialysis: One-Year Outcome Analysis in 394 Hemodialyzed Patients

Junnichi Ishii, Takanobu Toriyama, Masanori Nomura, Hiroyuki Naruse, Yoshihisa Mori, Masaki Yokoya, Yoshitaka Kumada, Hiroshi Takahashi, Hirohisa Kawahara, Yoshihiko Watanabe, Hitoshi Hishida. *Fujita Health University, Toyoake, Japan, Nagoya Kyoritsu Hospital, Nagoya, Japan*

A recent study has suggested that, in patients on chronic hemodialysis, the increased serum level of cardiac troponin T (cTnT) measured by the current cTnT assay originates from the heart, not from skeletal muscle expression of cTnT. To evaluate the prognostic value of increased serum cTnT in patients on chronic hemodialysis, we prospectively studied 394 consecutive patients (mean age 61 yrs; range 30 to 90 yrs; mean period of dialysis 8.0 yrs; range 0.5 to 25 yrs) on chronic hemodialysis without acute coronary syndrome in March of 1999. We measured serum cTnT by second-generation assay, serum heart-type fatty-acid binding protein (FABP) and plasma brain natriuretic peptide (BNP) in pre-dialysis samples. All patients were followed for 1 year. The cutoff value for cTnT was 0.10 ng/mL, 9 ng/mL for FABP, and 18.4 pg/mL for BNP. **Results:** cTnT was increased in 151 patients (38%), FABP in 394 (100%), BNP in 393 (99.7%). During the 1-year follow-up period, 31 (8%) cardiac events (19 deaths, 12 coronary artery disease requiring PTCA) occurred. Patients with cardiac events were older (p=0.0007), had higher levels of cTnT (p=0.0003) and BNP (p=0.0042), and a more frequent history of diabetes (p=0.0063)(Table). In a stepwise Cox regression analysis including cTnT, FABP, BNP, age, period of hemodialysis and history of diabetes, cTnT (RR 13.4, p=0.006), age (RR 1.05, p=0.016) and history of diabetes (RR 2.42, p=0.002) were independent predictors of cardiac events. The rate of cardiac events in patients with elevated cTnT was higher than in those without elevated cTnT [15% (23/151) vs 3% (8/243), p<0.0001]. **Conclusion:** These findings indicate that an elevated cTnT level is a potential prognostic marker of adverse outcome within 1 year in patients on chronic hemodialysis. cTnT could be reasonably included in the routine risk stratification of this population.

Data are mean±SD. *p<0.01 vs CEs(-). CEs=cardiac events.

	Age (yrs)	cTnT (ng/mL)	FABP (ng/mL)	BNP (pg/mL)	Diabetes (%)
CEs (+) (n=31)	67.2±8.8*	0.18±0.14*	87±24	1082 ± 1332*	42%*
CEs (-) (n=363)	60.2±11.2	0.10±0.10	80±32	553 ± 948	21%

1050-101 Prediction of Coronary Heart Disease in African-Americans and Whites Using Multiple-Risk-Factor Assessment Equations

Herbert J. Marx, Henry F. C. Weil, Thomas A. Pearson, Edward F. Philbin, Tara A. Erb, Paul L. Jenkins, Charles K. Francis, Roberta G. Reed. *Mary Imogene Bassett Hospital, Cooperstown, NY, Harlem Hospital, New York City, NY*

Background: American Heart Association (AHA)/American College of Cardiology (ACC) coronary heart disease (CHD) multiple-risk-factor assessment equations were derived from the Framingham Study which largely involved whites (W) of European origin. In the past, extension of similarly derived risk prediction models to other ethnic groups yielded mixed results.
Method: Applicability of the AHA/ACC risk assessment method to African-Americans (AA) was evaluated by determining global CHD risk factor scores (RFS) for a series of patients with no prior documented CHD who underwent diagnostic coronary angiography at Harlem and Bassett Hospitals. Risk factors consisted of age, total cholesterol. HDL-C, hypertension, diabetes, and smoking history. Subjects were categorized by angiography into those with ≥50% stenosis in a major coronary artery (CHD) and those with ≤ 25% stenosis (NL).
Results: There were no significant differences in overall average age or RFS between 79AA and 140W males (M) or between 64AA and 97W females (F). However, those with CHD had significantly higher RFS compared with NL (see table).

RFS ± SD	AAM	WM	AAF	WF
CHD	7.9±3.3	8.0±2.7	12.5±3.9	11.6±4.4
NL	5.3±3.3	5.1±3.1	8.0±2.7	7.9±6.5
p value	0.001	0.0001	0.058	0.005

Predicted relative risk was below average for NL in all 4 subgroups. For those with CHD, it was moderately above average for age for F and average for M.
Conclusion: AHA/ACC multiple-risk-factor assessment equations were equally applicable to AA and W of both genders in our cohort with higher RFS among those with CHD compared with NL. Relative risk was below average for NL in each subgroup and average to moderately high for those with CHD.

1050-102 Effect of Alcohol Consumption on Endothelial Function in Men With Coronary Artery Disease

Hiroki Teragawa, Yukihiro Fukuda, Keiji Matsuda, Kenya Sakai, Sou Takenaka, Fumiharu Miura, Hidekazu Hirao, Togo Yamagata, Hideo Matsuura, Kazuaki Chayama. *Hiroshima University, Hiroshima, Japan*

Background: An inverse association between moderate alcohol consumption and coronary artery disease (CAD) has been observed in several epidemiological studies. Although some possible mechanisms have been proposed, it is unknown whether endothelial function is associated with the beneficial effects of alcohol consumption. Therefore, we investigated the effects of alcohol consumption on endothelial function of the brachial artery in men with CAD. **Methods:** Forty-five men (mean age 65 yrs) with CAD, who had 50% stenosis of the major coronary arteries on coronary angiogram were evaluated. Alcohol consumption was defined as alcohol intake on 4 days per week. The patients were divided into two groups based on whether they consumed alcohol (Group I) or not (Group II), and flow-mediated dilation (FMD), an indicator of the brachial artery diameter in response to hyperemic flow, was measured using high resolution ultrasound (10MHz). Other parameters, including metabolic ones, were also measured. **Results:** Data are presented as mean±SEM. Twenty patients consumed alcohol (Group I). The level of lipids such as total cholesterol, triglycerides, high-density lipoprotein cholesterol and low-density lipoprotein cholesterol did not differ between the 2 groups, but the level of fasting blood sugar tended to be higher in Group I (121±10 vs 99±3 mg/dl in Group II, p = .0504). FMD was higher in Group I than in Group II (3.0±0.3 vs 2.1±0.3 %, p = .0309). Multivariate analysis showed that alcohol consumption (p = .0026) as well as brachial artery diameter after the administration of nitroglycerin (p = .0057) and the number of diseased vessels (p = .0343) influenced the FMD. **Conclusions:** These findings suggest that alcohol consumption may favorably influence endothelial function in men with CAD although it may affect some metabolic factors.

POSTER SESSION

1051 Coagulation and Inflammation in Acute Myocardial Infarction: Basic Observations

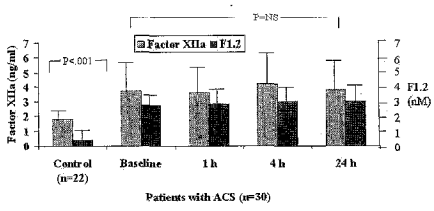
Sunday, March 18, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 4:00 p.m.-5:00 p.m.

1051-77 Factor XII Activation in Acute Coronary Syndromes: Fundamental Basis for Pharmacological Targeting of the Intrinsic Coagulation Cascade

Richard C. Becker, You Fu Li, Frederick A. Spencer. *University of Massachusetts Medical School, Worcester, MA*

Background: The pathobiology of acute coronary syndromes (ACS) is characterized by plaque disruption, injured site thrombosis and microcirculatory embolization. Although tissue factor (TF) is a dominant protein in atherothrombosis, the contribution of contact-activating factors and the physiologic integration of coagulation pathways must also be

considered as potential targets for pharmacologic treatment. **Methods:** Patients with non-ST segment elevation ACS (n=30) underwent serial blood sampling and were compared with age-matched controls (n=22) for markers of contact activation (factor XIIa) and thrombin generation (F1.2). The results were as follows:



In a series of in vitro experiments using western blot assays and densitometry, TF and/or TF-VIIa augmented intrinsic X^{ase} (factors IXa, VIIIa)-mediated thrombin generation, but had no effect on factor XII activation. In contrast, thrombin readily activated factors XII, IX and VIII. **Conclusion:** The bioamplification sequence of thrombin generation in ACS includes coagulation cascade "cross-talk" and upstream events involving contact activation. The pharmacologic inhibition of factor XIIa and its overall impact of modulating arterial thrombosis requires further clinical investigation.

1051-78 Regulation of Monocyte Procoagulant Activity in Acute Myocardial Infarction: Role of Tissue Factor and Tissue Factor Pathway Inhibitor

Ilka Ott, Martin Andrassy, Dominik Zieglgänsberger, Stefanie Geith, Valerie Malcouvier, Franz-Josef Neumann. *1. Medizinische Klinik und Deutsches Herzzentrum der TU München, Munich, Germany*

Background: In acute myocardial infarction (AMI), monocyte procoagulant activity is increased and may contribute to the risk of recurrence and other thrombotic events. This study sought to investigate the role tissue factor (TF) and its counterpart tissue factor pathway inhibitor-1 (TFPI-1) in the regulation of monocyte procoagulant activity in AMI. **Methods:** In 40 patients with AMI undergoing revascularization by stent placement, we obtained serial venous blood samples. Twenty patients with elective stenting for stable angina served as control subjects. We measured TF proteolytic activity with spectrozyme factor Xa (FXa), TF and TFPI-1 surface expression of monocytes by flow cytometry, mRNA expression by reverse transcription polymerase chain reaction, and concentrations of prothrombin fragments F1+2 by immunoassay. **Results:** Forty-eight hours after AMI, we found an increase in TF transcription followed by an increase in TF surface expression by 24+4% and in plasma concentration of prothrombin fragments F1+2 by 103+17% at 96 hours ($p<0.05$). These changes could not be attributed to the intervention, as they did not occur in the control group. TFPI-1 transcription and binding to the monocyte surface remained unchanged. In vitro, FXa generation by monocytes of patients with AMI was increased 3-fold in the presence of polyclonal antibodies to TFPI-1, indicating that cell-associated TFPI-1 inhibited monocyte TF activity. **Conclusion:** The increased monocyte procoagulant activity in AMI is caused by upregulation of TF that is only partially inhibited by surface-bound TFPI-1. Anticoagulant therapy by direct inhibition of TF activity may, thus, be particularly effective in AMI.

1051-79 Prevalence of C-reactive Protein in Unstable Versus Stable Angina Atheroma: Correlation With Persistency of Chlamydia Pneumoniae

Gerhard Bauriedel, René Andrié, Dirk Skowasch, Peter Braun, Karl W. Heinrich, Berndt Lüderitz. *Department of Cardiology, University of Bonn, Bonn, Germany, Heart Center Duisburg, Duisburg, Germany*

Background: There is increasing evidence that inflammation, infection and immune reactions play an important role in the acuity/progression of atherosclerosis. Therefore, we sought to detect C-reactive protein (CRP), chlamydial heat schock protein 60 (cHSP 60) indicating persistency of *Chlamydia pneumoniae* infection, and human (h) HSP 60 that serves as a target for autoimmune reactions, in primary lesions associated with unstable (UA) *vs.* stable angina (SA).
Methods: Coronary atherectomy samples retrieved from 45 primary target lesions of patients with UA (n=30) or SA (n=15) were immunohistochemically examined for the presence of CRP, cHSP 60 and hHSP 60. These data were correlated with plaque morphology and assessed for prevalence and correlation in either lesion group.
Results: Coronary plaques revealed immunoreactive CRP in 26 (58%), cHSP 60 in 29 (64%) and hHSP 60 in 36 (80%) of 45 lesions *vs.* none of 20 undiseased controls. Intimal predilection sites were areas with macrophage/foam cell accumulation, inflammatory infiltrates and sparse cellularity. Expression averaged to 1.8% for CRP, 6.6% for cHSP 60 and 6.5% for hHSP 60. As a key finding, consistently, the expression of each protein was significantly higher in UA compared to SA lesions. CRP: 2.3% *vs.* 1.1% ($p<0.05$); cHSP 60: 8.7% *vs.* 3.0% ($p<0.01$); hHSP 60: 8.7% *vs.* 2.0% ($p<0.001$). Moreover, we found positive correlations ($p<0.01$ each, n=45) for CRP/cHSP 60 (r=0.38), CRP/hHSP 60 (r=0.47) and cHSP 60/hHSP 60 (r=0.44). Subgroup analysis revealed correlations ($p<0.05$) for CRP/cHSP 60 (r=0.38) and cHSP 60/hHSP 60 (r=0.35) only in lesions associated with UA.
Conclusion: Specific markers of inflammation and infection are colocalized within coronary atheroma, the more in primary lesions associated with UA. Intimal persistency of *C. pneumoniae* may be an important chronic stimulus for inflammatory and/or stress events involved in plaque rupture.

1051-80 Endogenous Fibrinolytic Activity and Response to Thrombolytic Therapy in Acute Myocardial Infarction

David E. Newby, Nicholas L. M. Cruden, Laura L. Flint, Nicholas A. Boon, Keith A. A. Fox. *University of Edinburgh, Edinburgh, United Kingdom*

Background Impaired endogenous fibrinolysis may contribute to the pathogenesis of acute myocardial infarction. We postulated that the efficacy and rapidity of reperfusion of the infarct-related artery with exogenous thrombolytic therapy would be enhanced in those patients with low endogenous plasma tissue plasminogen activator (t-PA) activity. **Methods** Admission fibrinolytic parameters were determined in 59 patients, aged 65 ± 2 years (42 male), with acute myocardial infarction who fulfilled clinical and electrocardiographic criteria for thrombolytic therapy. Continuous ST segment monitoring was performed, and aspirin and thrombolytic therapy administered. Reperfusion was defined as a fall in the ST segments of *50 % or new onset idioventricular rhythm. **Results** Reperfusion occurred in 39 (66%) patients 91 ± 8 min after the initiation of thrombolytic therapy and was associated with a lower admission plasma t-PA activity concentration (1.4 ± 0.2 vs 2.5 ± 0.5 IU/mL, p=0.03). Reperfusion time directly correlated with admission plasma t-PA activity (r=0.47, p=0.003). **Conclusions** We have shown that patients who fail to reperfuse with thrombolytic therapy have higher admission plasma t-PA activity suggesting the presence of t-PA resistant occlusion of the infarct-related artery. However, in patients who reperfuse, lower plasma t-PA activity is associated with a more rapid response to thrombolytic therapy suggesting that patients with impaired endogenous fibrinolysis benefit most from thrombolytic therapy.

1051-81 Absence of Interaction Between Clopidogrel and Warfarin in Patients on Long-Term Anticoagulation

C Lidell, L-E Svedberg, P Lindell, S Bandh, L Wallentin. *Department of Cardiology, Uppsala University Hospital, Uppsala, Sweden*

Background: Clopidogrel (C), an ADP receptor antagonist, is indicated for secondary prevention in patients with recent ischaemic stroke, recent myocardial infarction or peripheral arterial disease. Warfarin may be used in patients with atherothrombosis, in circumstances which are associated with a history of myocardial infarction or ischaemic stroke. A randomized, double-blind, placebo-controlled, parallel group trial to test for a possible interaction between C and warfarin was conducted.
Methods: Main inclusion criteria were: age 35–75 years; receiving long-term (> 2 months) warfarin treatment for chronic or recurrent non-valvular atrial fibrillation (NVAF), with an INR value remaining between 2 and 3 under constant warfarin regimen, as confirmed by 3 weekly controls performed during a run-in period. Patients were randomly assigned to C 75 mg QD ($n \approx 20$) or matching placebo ($n = 23$) administered for 8 days (Days 1–8) on top of the constant warfarin regimen. Follow-up was continued until Day 22. The primary endpoint was percent change in INR from baseline through the overall evaluation period including Days 3, 6, 9, 13 and 22. The secondary endpoint was percent change in plasma levels of warfarin enantiomers from baseline at the same time points. Plasma levels of C metabolite SR26334 were also assayed to confirm observance.
Results: Mean INR remained extremely stable under C, the maximum percent change from baseline being 0.6% at Day 6. There was no statistically significant difference between the two treatment groups in the percent change from baseline at any time point. All the 95% confidence intervals remained between 2.28 and 2.72, and a greater than 5% increase in INR under C could be ruled out. Plasma levels of R- or S-warfarin remained also very stable under C. No serious adverse events were reported during the study, and there were no premature discontinuations of study drug. No bleeding occurred under C.
Conclusions: The stable anticoagulation status of patients on long-term warfarin therapy is not modified by concomitant administration of clopidogrel 75 mg QD . Safety and tolerability of such combination were good in this study.

1051-82 Interleukin-6 G-174C Polymorphism Is Associated With Occurrence of Unstable Angina and With In Vitro Increased Monocyte Production of Interleukin-6 in Unstable Patients

Luigi M. Biasucci, Dominick J. Angiolillo, Pier Franco Pignatti, Chiara Stranieri, Vittoria Rizzello, Christian Colizzi, Giovanna Liuzzo, Attilio Maseri. *catholic university, Rome, Italy, University of verona, Verona, Italy*

Background: Interleukin-6 (IL-6), the main inducer of C-Reactive protein (CRP) production, is raised in acute coronary syndromes. A common polimorphism G-174C of the human IL-6 gene in the 5' region has been described. In normal subjects the G allele has been associated with higher IL-6 plasma levels. Aim of this study was to assess the role of the G-174C polimorphism in unstable angina (UA). **Methods:** We studied 52 patients with UA, Braunwald's class IIIB, (29 with CRP>3mg/L and 23 with CRP<3mg/), and 17 patients with stable angina. All patients were genotyped for the G-174C. In 23 of these patients 1 mL of whole blood was stimulated in vitro with 1ng lipopolysaccaride, and IL-6 was measured 4 hours after stimulation to assess the monocyte response. **Results:** The frequency of the G allele was higher in UA (81%) versus stable angina (62%, p=0.02), but no significant difference was observed between UA with high or low CRP levels. After LPS stimulation of whole blood in vitro, G homozygote patients (n=15) had higher IL-6 levels than heterozygotes (n=8): median levels were respectively 4,435 (range 670-10,583) and 2,000 (range 75-4,790) picogr/ml (p=0.05) **Conclusion:** Our data demonstrate that the G allele of the G-174C polymorphism of IL-6 is associated with unstable

angina and is associated with an increased monocyte production of IL-6 in vitro. The G allele of the G-174C polimorphism appears associated with unstable angina, possibly in part via an enhanced production of IL-6 in response to inflammatory stimuli.

1051-83 A Polymorphism in the Promoter of the CD14 Receptor Gene Is Associated With Circulating Soluble CD14 Levels and With an Enhanced Pro-Inflammatory Response in Patients With Unstable Angina

Giovanna Liuzzo, Dominick J. Angiolillo, Pier F. Pignatti, Chiara Stranieri, Matteo Santamaria, Vittoria Rizzello, Francesca Ginnetti, Antonino Buffon, Luigi M. Biasucci, Attilio Maseri. *Catholic University, Rome, Italy*

Background: Activation of circulating monocytes (MO) has been shown in unstable angina (UA). The CD14 membrane receptor is an important mediator for MO activation by bacterial lipopolysaccharide (LPS). CD14 is also present in a soluble form (sCD14), and sCD14 levels are strongly associated with prognosis in gram-negative infections. A C(-260) T polymorphism in the promoter of the CD14 receptor gene was recently associated with increased risk of myocardial infarction. In this study, we examined whether the C(-260) T polymorphism in the CD14 gene influenced sCD14 levels, the activation of circulating MO and the acute phase response in UA. **Methods:** Plasma levels of sCD14 and C-reactive protein (CRP), and interleukin-6 (IL-6) production by circulating MO after in vitro stimulation of whole blood with a low dose of LPS (1ng/mL, for 4 hours) were compared in 44 UA patients, 35 stable angina (SA) patients and 20 healthy subjects (C). The CD14 C(-260) T polymorphism was assessed in 26 UA, 12 SA and 12 C. **Results:** Data are presented as median. Plasma levels of sCD14 were significantly higher in UA (2.5 mcg/mL) than in SA (2.2 mcg/mL) and C (2 mcg/mL) (P<0.05). LPS-stimulated production of IL-6 by circulating MO was significantly higher in UA (4.4 ng/mL) than in SA (1.9 ng/mL) and in C (0.5 ng/mL) (P<0.01). A positive linear correlation was observed between plasma levels of sCD14 and CRP (r=0.42, P<0.01), as well as between sCD14 and IL-6 production in response to LPS (r=0.38, P<0.01). TT homozygotes had significantly higher sCD14 levels (2.4 mcg/mL) than carriers of both the CC (2.1 mcg/mL) and CT (1.8 mcg/mL) genotypes (P<0.05). TT homozygotes also showed increased production of IL-6 by circulating MO in response to LPS-challenge (4.0 ng/mL) than carriers of the other two genotypes (1.9 and 1.3 ng/mL, respectively; P<0.05). **Conclusion:** Circulating MO of UA patients exhibit an enhanced responsiveness to LPS-challenge, which is related to sCD14 plasma levels, the soluble form of the receptor for bacterial LPS, and to a polymorphism in the promoter of the CD14 receptor gene. Our data suggest that a genetically determined response of circulating MO to infectious stimuli may contribute to determine the inflammatory component in UA.

POSTER SESSION

1052 Acute Coronary Syndromes: Plasma Markers and Prognostic Studies

Sunday, March 18, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 4:00 p.m.-5:00 p.m.

1052-84 Cardiac Troponin I Is A Powerful Long-Term Predictor of Serious Cardiac Events: Follow-Up of 501 Patients for 35 Months

Graham Hillis, Pamela Taggart, Lorraine Hillis, Ning Zhao, Antoinette Mangione. *Albert Einstein Medical Center, Philadelphia, PA*

Background: Sensitive and specific cardiac markers are excellent predictors of early outcome in patients with chest pain. There are, however, few data regarding the relative utility of such markers in predicting the long-term outcome of such patients. The aim of the current study was to assess the relative prognostic ability of clinical factors, cardiac troponin I (cTnI), creatine kinase MBmass (CK-MBmass), myosin light chain 1 (MLC-1) and myoglobin (Mgb). **Methods:** Five hundred and one patients presenting with chest pain were studied prospectively. Eligibility criteria included > 15 minutes of chest pain at rest within the prior 24 hours felt clinically to represent myocardial ischemia, but with clinical and ECG features on admission suggesting a low risk of acute myocardial infarction (AMI). Cardiac TnI, CK-MBmass, MLC-1 and myoglobin levels were assayed at presentation (0 hours) and at 6 and 12 hours. These were performed by technicians blinded to all clinical data and were not available to the clinicians treating study subjects. Patients were followed up a median of 35 (range 9 – 49) months later. The primary study end-point was the occurrence of a serious cardiac event (SCE: death, non fatal AMI or coronary revascularization) after the index admission. The relative predictive values of different markers and clinical factors (age, sex, current smoker, history of hypertension, history of diabetes history of coronary revascularisation) were assessed using logistic regression. **Results:** Follow-up data were available on 488 patients (97%), of whom 99 (20%) suffered an SCE during follow-up. All four biochemical markers were significant predictors of the occurrence of an SCE during follow-up. Cardiac TnI was, however, the most powerful (OR 3.5, 95% CI 2.0-6.3; p < 0.0001) and only independent biochemical predictor. In a multivariate logistic regression equation, age was the only other independent predictor (OR 1.03 per year, 95% CI 1.01-1.05; p = 0.006). **Conclusions:** The current data confirm that cTnI is a powerful independent predictor of long-term adverse events in patients with chest pain. In this respect it is superior to other widely available cardiac markers and most clinical parameters.

1052-85 Improved Risk Stratification of Patients With Unstable Angina Using a Lower Than Usual Cut-Off Point of Troponin T Combined With CK-MB Measurement

B. Charles Solymoss, Martial G. Bourassa, Peter Cernacek, André Couturier, Pierre Théroux. *Montreal Heart Institute, Montreal, PQ, Canada*

Unstable angina (UA) pts with > or = 0.1 µg/L cardiac Troponin T (cTnT) levels have a higher risk of future coronary events than those with lower values. We examined, in 131 pts (Age: 65.5±11.8; Female: 48), with < 24 hrs episode of UA whether a lower cTnT cut-off point, combined with CK-MB measurement, improves risk stratification. Plasma samples, obtained upon arrival and at 4, 8, and 12 to 24 hours, were analyzed with Elecsys 1010 and the second generation of cTnT reagents. Peak values were correlated with a composite endpoint of new episodes of cTnT-positive UA, myocardial infarction (MI) or death during a mean follow-up of 15 (range 13 to 17) months. The risk of events was evaluated using the usual cTnT cut-off point (> or = 0.1 µg/L), and a lower cut-off point (> or = 0.04 µg/L). cTnT positive pts were further subdivided according to CK-MB values (< vs. > or = 5.0 µg/L). At baseline, risk factors and history of MI, PCI or CABG were not different between these groups. During the follow-up, 48 pts (36.6%) underwent PCI or CABG with no significant differences in frequency between groups. Using the > or = 0.1 µg/L cTnT cut-off point, the frequency of subsequent events was 8/71 (11.3%) with negative cTnT, 4/27 (14.8%) with positive cTnT but negative CK-MB, and 11/33 (33.3%) with both markers positive (overall, p = 0.0207; negative vs. positive CK-MB, p < 0.09). With the lower (> or = 0.04 µg/L) cTnT cut-off point, the respective figures were 2/46 (4.3%), 6/43 (14%) and 15/42 (35.7%) (overall, p = 0.0004; negative vs. positive CK-MB, p = 0.02). Thus, the use of a lower cut-off point for cTnT values and the additional analysis of CK-MB further improves the risk stratification of UA pts.

1052-86 High-Sensitivity C-Reactive Protein (hs-CRP) to Predict 6 Month Mortality and Relative Benefit of Invasive vs. Conservative Strategy in Patients With Unstable Angina: Primary Results of the TACTICS-TIMI 18 C-Reactive Protein Substudy

Christopher P. Cannon, William S. Weintraub, Laura Demopoulos, Ralph Vicari, Oscar Bazzino, Nadir Ali, Debbie Robertson, Paul DeLucca, Peter DiBattiste, Nader Rifai, Eugene Braunwald, for the TACTICS-TIMI 18 Investigators. *Brigham and Women's Hospital, Boston, MA*

Recent studies have found that high-sensitivity C-reactive protein (hs-CRP) is a potent marker of adverse prognosis in unstable angina and non-ST elevation MI. We sought to validate this marker in a large cohort of patients and to assess the usefulness of hs-CRP in predicting benefit of an invasive vs. conservative strategy. **Methods:** In the TACTICS-TIMI 18 trial patients with unstable angina or non-ST elevation MI were treated with aspirin, heparin and tirofiban and randomized to an invasive strategy with routine catheterization and revascularization within 4-48 hours, or to a conservative (i.e., a "selective invasive" strategy) with catheterization performed only if the patient had objective evidence of recurrent ischemia or a positive stress test. Hs-CRP (Dade-Behring) was measured in all patients who provided a baseline blood sample (N=1804). **Results:** Preliminary results as of August 2000 showed a higher 6-month mortality rate for those with hs-CRP> 1.5 mg/dl (99th percentile of normals).(See Table) Similarly, death or MI, and the primary endpoint of death, MI or rehospitalization for acute coronary syndrome were significantly higher among patients with hs-CRP > 1.5.

hs-CRP	<= 1.5	> 1.5	P value
N=	1396	408	
Mortality (%)	2.08	6.37	<0.001
Death/MI (%)	6.66	11.03	0.004
Composite (%)	15.7	20.6	0.02

Conclusion: In this large cohort of patients with unstable angina, hs-CRP was a significant predictor of 6-month mortality, and recurrent cardiac events. Its use in predicting benefit of a routine invasive vs. "selective invasive" strategies will be presented.

1052-87 Six Month Prognosis After Hospital Discharge in Patients With Acute Coronary Syndromes: The GRACE Project

Robert J. Goldberg, Frederick Spencer, Joel M. Gore, Immad Sadiq, Cynthia Sullivan, Keith Fox, Gabriel Steg, Kim Eagle, Christopher Granger, Alvaro Avezum. *University of Massachusetts Medical School, Worcester, MA*

Background: The acute coronary syndromes (ACS) continue to be a major reason for hospital admissions with significant attendant morbidity and mortality. While significant advances have been made in improving the hospital outcome for these patients, considerably less information is available about the long term prognosis for this group of patients.

Methods: The Global Registry of Acute Coronary Events (GRACE) Registry is enrolling patients with ACS at 94 hospitals in 14 countries. In addition to detailed information on inhospital treatment and selected short-term outcomes, patients have follow-up data collected at 6 months following hospital discharge assessing the development of subsequent coronary events and medication adherence.

Results: To date, 2795 patients with ACS have been successfully followed since hospital discharge. This includes 1576 patients with myocardial infarction (MI)(880 with ST segment elevation [STE] MI and 696 with non-STE MI), 1067 with unstable angina, and 122 with other cardiac diagnoses. The 6 month post discharge death rates were highest in those with non STE MI (7.3%), followed by patients with STE MI (5.9%), those with unstable angina (4.9%) and those with other cardiac discharge diagnoses (4.1%). Rehospitalization rates for heart disease were relatively frequent (~20%) in all patient groups. Results of a multivariable regression analysis controlling for various demographic

and clinical characteristics revealed that older patient age and failure to receive ACE inhibitors at the time of hospital discharge were significantly associated with 6 month death rates in patients with AMI and unstable angina. Older patient age and failure to receive beta blockers or statins were associated with significantly increased risk of rehospitalization in patients with ACS.
Conclusions: Our results from a multi-hospital, multi-country registry suggest that patients discharged from the hospital with ACS continue to experience significant morbidity and mortality over the ensuing 6 months. Targeted interventions need to be directed to the elderly and to the increased use of evidence-based proven therapies to improve prognosis after ACS.

1052-88 Optimal Discriminative Value of Troponin-I for 6 Month Cardiac Event Rate in the Evaluation for Suspected Acute Coronary Syndromes

Vincent Roolvink, Hans E. Luijten, Marc A. Brouwer, Gérard J. H. Uijen, Ries de Keijzer, Tjeerd van der Werf, Freek W. A. Verheugt. *Heartcenter, University Medical Center, Nijmegen, The Netherlands*

Background. Troponin-I (cTnI) has proven to be a useful prognostic marker for short-term outcome in patients presenting with a suspected acute coronary syndrome. Nevertheless, a fair amount of patients with a positive cTnI (> 0.20 ng/ml) will not develop a major ischemic event. This study sought to assess the optimal discriminative value of cTnI with respect to long-term outcome.
Methods. Between January 1, and October 31, 1999, cTnI-levels were determined 8 hours or more after symptom onset in 150 patients presenting with acute chest pain at the emergency department. Clinical charts were reviewed for subsequent events: cardiac death(†), (re-)infarction(reMI), revascularization (revasc.) and recurrent angina (reAP). cTnI-levels were assessed by discriminant analysis, with respect to the optimal combination of positive- and negative predictive value (P.P.V. ; N.P.V.), sensitivity (SN) and specificity (SP).
Results. Mean follow-up time was 235 ± 85 days. Optimal cTnI levels for the respective clinical endpoints are given in the table. The rate of †/reMI was 2% in case of a cTnI < 0.36 ng/ml (n=112): 14% for patients with a cTnI between 0.20 and 0.36 ng/ml (n=14), in contrast to 0% in patients with a cTnI < 0.20 ng/ml (n=98).
Conclusions. According to these findings, even a cTnI level slightly higher than 0.20 ng/ml carries a markedly increased risk for death and reinfarction within 6 months after the index event.

	N (%)	cTnI (ng/ml)	P.P.V.	N.P.V.	SN	SP
cardiac death (†)	3 (2%)	0.42	5%	99%	67%	76%
†/reMI	10 (7%)	0.36	22%	98%	80%	79%
†/reMI/revasc.	38 (25%)	0.23	58%	90%	74%	82%
†/reMI/revasc./reAP	52 (35%)	0.20	71%	85%	71%	85%

POSTER SESSION

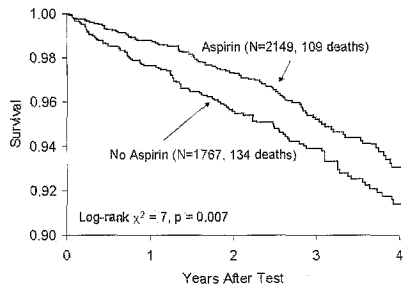
1053 Cardioprotection During Myocardial Infarction

Sunday, March 18, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 4:00 p.m.-5:00 p.m.

1053-89 Aspirin Use and All-Cause Mortality Among Patients Being Evaluated for Known or Suspected Coronary Artery Disease: A Propensity Analysis

Patricia A. Gum, Maran Thamilarasan, Junko Watanabe, Eugene Blackstone, Michael S. Lauer. *Cleveland Clinic, Cleveland*

Background: Although aspirin has been shown reduce cardiovascular morbidity, the association between its use and long-term all-cause mortality has not been well defined.
Methods: We prospectively studied 6527 consecutive adults referred for stress echocardiography at the Cleveland Clinic between 1990 and 1998 for evaluation of known or suspected coronary disease; 2455 (38%) were taking aspirin. We used propensity analysis to identify patients for whom comparisons between aspirin use and no aspirin use were valid and to account for selection biases. **Results:** During 3.1 years of follow-up, 310 patients (5%) died. After adjustment for age, gender, standard risk factors, use of other medications, coronary disease history, ejection fraction, functional capacity, heart rate recovery, and echocardiographic ischemia, aspirin use was associated with reduced mortality (hazard ratio [HR] 0.65, 95% confidence interval [CI] 0.51-0.84, p=0.0008). According to a propensity analysis, there were 3916 patients for whom comparisons between aspirin users and non-users were valid; among these patients 2149 (55%) were taking aspirin. During follow-up there were 243 deaths (6%). Patients taking aspirin were at lower risk for death (5% vs 8%, HR 0.71, 95% CI 0.55-0.91, p=0.007). See Figure. After adjusting for the propensity for using aspirin, as well as all other possible confounders and interactions, aspirin use remained associated with a lower risk for death (adjusted HR 0.68, 95% CI 0.52-0.89, p=0.005). **Conclusion:** In this propensity analysis, the use of aspirin among patients undergoing stress echocardiography for evaluation of known or suspected coronary artery disease was independently associated with reduced long-term all-cause mortality.



1053-90 Cardioprotective Effects of Intravenous Infusion of Magnesium Sulphate in Acute Myocardial Infarction

Hiroshi Nakashima, Toshirou Katayama, Yukiharu Honda, Shin Suzuki. *Department of Cardiology, Nagasaki Citizens Hospital, Nagasaki, Japan*

Background: The role of magnesium (Mg) in treating acute myocardial infarction (AMI) is controversial. Two major clinical trials (LIMIT 2, ISIS-4) which have attempted to examine the efficacy of Mg in AMI have produced conflicting results with respect to mortality. Experimental studies have however shown that intravenous Mg started before reperfusion produces beneficial effects by decreasing infarct size and suppressing free radicals.
Methods: We randomly divided 98 patients with a first AMI (anterior or inferior location) into two groups, an Mg (n=48) and a control groups (n=50). All patients were successfully reperfused by primary PTCA. Before reperfusion, Patients in the Mg group received a bolus injection of 8 mmol Mg sulphate followed by an infusion of 32 mmol over 24 h. Left ventriculograms prior to discharge were used to evaluate ejection fraction (EF) and end-diastolic volume index (EDVI) by the area-length method. Regional wall motion (RWM) in infarcted segments was analyzed using the centerline method. Coronary flow reserve (CFR) in the infarct-related artery was measured to assess coronary microvascular function, using a Doppler guidewire. CFR was expressed as the ratio of maximal hyperemic average peak velocity after injection of intracoronary papaverine to the baseline value.
Results: There was no significant difference between the groups in the time to reperfusion. Distribution of culprit lesion location, diseased vessels, and collateral grade were similar between the groups. The frequency of the angiographical no reflow phenomenon was significantly higher in the control group than in the Mg group (10% vs 0%). Left ventricular EF, EDVI and RWM were significantly better in the Mg group than in the control group (EF:63±9 vs 53±13 %, p<0.001; EDVI:57±14 vs 72±21 mL/m2, p<0.001; RWM:-0.90±1.30 vs Ð1.83±1.15 SD/chord, p=0.002). CFR was also significantly higher in the Mg group than in the control group(2.9±0.8 vs 2.4±0.9, p=0.036). **Conclusions:** Intravenous Mg sulphate started before reperfusion may preserve left ventricular systolic function and suppress dilatation, and result in better coronary microvascular function compared to reperfusion alone in patients with AMI.

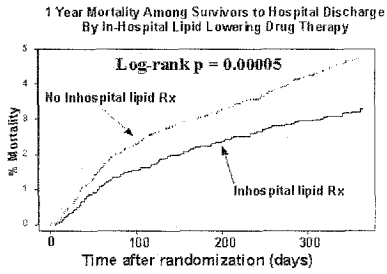
1053-91 Lipid Lowering Drug Therapy Initiated During Hospitalization for Acute MI is Asociated With Lower Postdischarge 1-Year Mortality

Robert P. Giugliano, Elliott M. Antman, Susan L. Thompson, Carolyn H. McCabe, Eugene Braunwald. *Brigham and Women's Hosital, Boston, MA, Nottingham Clinical Research Group, Nottingham, United Kingdom*

Background – The benefit of commencing lipid lowering drug therapy (LLRx) during hospitalization for AMI has not been established.
Methods – We analyzed baseline characteristics, concomitant treatments, inhospital complications, and 1-yr mortality among 14,124 patients with AMI surviving the index admission in InTIME-II, a randomized double-blind trial comparing tPA and nPA. The association between the use of LLRx with 1-yr mortality, adjusted for baseline characteristics and inhospital complications (recurrent MI, CHF, shock, stroke), was explored in a multivariate model.
Results - 34.3% of patients who survived to discharge received LLRx inhospital. Unadjusted 1-yr mortality post-discharge was 33% lower among patients receiving inhospital LLRx (3.0% vs. 4.5%, p = 0.00005). After multivariate adjustment, inhospital LLRx was associated with 20-36% lower mortality 1-year post-discharge:

Prior Lipid Rx	In hospital Lipid Rx	OR	95% CI	p-value
No	No	1.0	referent	group
Yes	No	1.05	0.61-1.83	0.86
No	Yes	0.80	0.63-1.22	0.07
Yes	Yes	0.64	0.43-0.97	0.03

Conclusions – LLRx during the index hospitalization is associated with improved survival in this observational study, and provides additional support for early initiation of LLRx following acute MI.



1053-92 Lower Myocardial Infarction Risk in Users of Selective Serotonin Reuptake Inhibitors

William H. Sauer, Jesse A. Berlin, Stephen E. Kimmel. *University of Pennsylvania School of Medicine, Philadelphia, PA*

Background: Depression is an independent risk factor for myocardial infarction (MI). Selective serotonin reuptake inhibitors (SSRIs) may reduce this risk via treatment of depression and attenuation of serotonin-mediated platelet activation. **Methods:** A case-control study of first MI in smokers, ages 30 through 65, was conducted among all 68 hospitals in an 8-county area during a 28 month period. Cases were smokers hospitalized with a first MI, and controls were randomly selected smokers from the same geographic area. Detailed information regarding medication use and other clinical and demographic data were obtained by telephone interview. Anxiolytic use served as an alternate exposure group to assess the potential for selection and recall bias. **Results:** 653 cases and 2,990 controls participated. After adjustment, using multivariable logistic regression, for age, gender, race, education, exercise, quantity smoked/day, body mass index, aspirin use for MI prevention, family history, and history of coronary disease, diabetes, hypertension, and hypercholesterolemia, the odds ratio (OR) for MI among SSRI users compared with non-antidepressant users was 0.32 (95% CI: 0.16, 0.62; P<0.01). A dose-response relationship towards reduced risk of MI was seen with increasing doses of SSRIs (P for trend <0.01). Non-SSRI antidepressant users had a nonsignificant reduction in MI risk with wide confidence intervals (adjusted OR 0.47, CI: 0.17, 1.29; P=0.14). However, analysis of this group was limited by the small number of exposed subjects. Anxiolytic use was not associated with MI (adjusted OR 0.96; CI: 0.56, 1.66; P =0.89). **Conclusion:** There is a significant association between SSRI use and MI protection. This may be due to a reduction in depression-associated MI risk and/or the inhibitory effect SSRIs have on serotonin-mediated platelet activation.

1053-93 Early Use of Beta-Blockers Is Associated With an Attenuation of Serum C-Reactive Protein Elevation and a Favorable Short-Term Prognosis After Acute Myocardial Infarction

Toshihisa Anzai, Tsutomu Yoshikawa, Toshiyuki Takahashi, Yuichiro Maekawa, Yasushi Asakura, Shiro Ishikawa, Hideo Mitamura, Satoshi Ogawa. *Keio University School of Medicine, Tokyo, Japan*

Background: Peak serum C-reactive protein (CRP) levels in patients with an acute myocardial infarction (AMI) is known to correlate well with peak serum IL-6 levels, but not with peak creatine kinase (CK) levels, suggesting that the serum CRP level may reflect the process of infarct healing. We have reported that an extreme elevation of serum CRP level is an independent predictor for cardiac rupture and left ventricular (LV) aneurysmal formation after AMI. Beta-blocker is shown to have a protective effect against cardiac rupture, however, the effect of beta-blocker on serum CRP elevation after AMI has not been determined. **Methods and Results:** We studied a total of 105 patients with first Q-wave AMI. Patients complicating pump failure (class>Killip 1 and/or subset>Forrester I) were excluded from this study. Forty-eight patients received beta-blocker (metoprolol, atenolol, or propranolol) treatment within 24 hours from the onset of AMI, while 57 patients received no beta-blocker treatment. Peak serum CK and CRP levels were determined by serial measurements (CK, every 6 hours; CRP, every 24 hours) and a prognosis was assessed in each group. There was no difference in age, gender, coronary risk factors, preinfarction angina, infarct site, the prior use of beta-blocker, the use of ACE inhibitor or calcium antagonists, the use of or success rate of revascularization therapy, and the prevalence of multivessel disease between the groups. Beta-blocker treatment was associated with a lower peak CRP level (8.1±1.0 vs. 11.7±1.3 mg/dl, p=0.04), a shorter duration from the onset to the peak CRP level (2.5±0.1 vs. 3.2±0.2 days, p<0.01) and a lower in-hospital cardiac mortality (0 vs. 9%; 4 patients with cardiac rupture and one patient with ventricular arrhythmia, p=0.03), despite similar peak CK levels (1829±381 vs. 1660±195 IU/l, p=0.67). **Conclusion:** The early use of beta-blocker is associated with decreased serum CRP level and a favorable short-term outcome after first Q-wave AMI, suggesting some beneficial effects of beta-blocker treatment on infarct healing after AMI.

1053-94 Cardioprotective Effect of Vasopeptidase Inhibitors in the Infarcted and Remodeling Rat Heart

Nathalie Lapointe, Charles Blais Jr, Albert Adam, Martin Sirois, Robert Clement, Hugues Gosselin, Jean L Rouleau. *Toronto General Hospital, Toronto, ON, Canada, University of Montreal, Montreal, PQ, Canada*

Background: Part of the cardioprotective effect of angiotensin converting enzyme inhibitors (ACEi) in the post-myocardial infarction (MI) setting, is thought to be due to attenuation of bradykinin (BK) metabolism. Vasopeptidase inhibitors (Vpi), by inhibiting both ACE and neutral endopeptidase (NEP), further reduce BK metabolism and increase natriuretic peptides and thus may have better cardioprotective effects than ACEi post-MI. **Methods:** MI was induced in by coronary ligation (n=514). Rats surviving 4 hours post-MI (n=255) were assigned to, the Vpi, omapatrilat (80mg/kg/day), omapatrilat (40 mg/kg/day), the ACEi captopril (160 mg/kg/day) or no treatment. After 56 days, hemodynamic measurements were done and rats were separated into two groups, one for remodeling (diastolic pressure-volume relations, morphometry) and the other one for biochemistry studies (mRNA was assayed by RTPCR). **Results:** Omapatrilat and captopril resulted in similar improvement in survival, hemodynamic measurements, and attenuated ventricular dilatation. The pattern of ventricular remodeling differed between omapatrilat and captopril, despite causing similar reductions in ventricular weights. Both interventions reduced expression of the pro-fibrotic cytokine TGF, neither effected the anti-inflammatory cytokine interleukin 10, and only captopril reduced the pro-inflammatory cytokine TNF a. Expression of TNF a was in cardiomyocytes. All groups reduced endothelin-1 levels, and only omapatrilat increased natriuretic peptides. **Conclusion:** This study indicates that both omapatrilat and captopril markedly improve post-MI survival, cardiac function and cardiac remodeling in the rat. Although minor differences exist between the effects of the two drug classes in the post-MI setting, it would appear that the addition of NEP inhibition to those of ACE inhibition does not result in significant further benefit.

POSTER SESSION

1054 Coronary Pathogenetic Aspects in Acute Coronary Syndromes

Sunday, March 18, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 4:00 p.m.-5:00 p.m.

1054-95 Platelet Glycoprotein (GP) IIb/IIIa Is Associated With Platelet Aggregation in Coronary Lesions Underlying Acute Coronary Syndromes

Takurou Shinsato, Takahiko Naruko, Makiko Ueda, Kazuo Haze, Akira Itoh, Masato Otsuka, Yuji Sakanoue, Yoshihiro Ikura, Masayuki Ogami. *Osaka City General Hospital, Osaka, Japan, Osaka City University Medical School, Osaka, Japan*

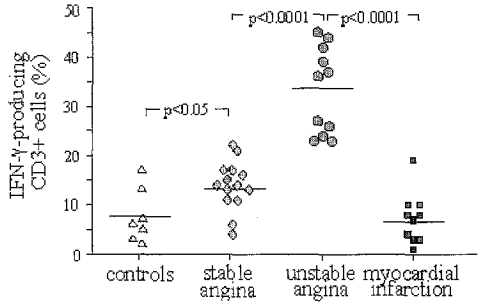
Background : Plaque rupture, hemorrhage,and thrombus formation have been implicated as the mechanisms responsible for transformation of stable coronary lesions into active lesions,leading to unstable angina pectoris (UAP) and acute myocardial infarction. Especially platelet aggregation at the site of plaque rupture or erosion is a dominant feature in the pathophysiology of plaque destabilization. To elucidate the role of GPIIb/IIIa in coronary plaque destabilization, we immunohistochemically studied the presence of GP IIb/IIIa in coronary atherectomy specimens obtained from patients with stable angina (SAP) and UAP. Moreover we immunohistochemically investigated the presence of P-selectin, which is known to be a marker of platelet activation, in these specimens. **Methods:** All these patients underwent atherectomy at primary atherosc lesions responsible for SAP (n=25) and UAP (n=23). Frozen samples were studied with antibodies against smooth muscle cells, macrophages (MAC), endothelial cells, GPIIb/IIIa (CD41) and P-selectin. Immunoreactive positive areas for GPIIb/IIIa, P-selectin, and MAC, respectively, were calculated as a percentage of the total area, using computer-aided planimetry. For the identification of cell types which stain positive for GPIIb/IIIa or P-selectin, immunodouble staining was also performed. **Results:** The percentage of GPIIb/IIIa, P-selectin and MAC positive area was significantly higher (P<0.001) in patients with UAP than in patients with SAP. In patients with UAP, 21 of 23 lesions (91%) contained GPIIb/IIIa positive platelet thrombi, and all these platelet thrombi were positive for P-selectin. In contrast, in SAP patients 10 of 25 lesions (40%) showed GPIIb/IIIa positive thrombi,and only 3 lesions (12%) revealed P-selectin positivity in platelet thrombi. **Conclusions:** These findings strongly suggest that platelet activation and aggregation,leading to formation of platelet thrombi,play an important role in plaque destabilization in human coronary atherosclerotic lesions.

1054-96 Expansion of Interferon-Gamma-Producing Th1 Lymphocytes as a Mechanism of Progression in Acute Coronary Syndromes

Jörg Koglin, Heiko Methe, Stefan Brunner, Daniela Wiegand, Wolfgang von Scheidt. *Medizinische Klinik 1, Universitätsklinikum Grosshadern, Munich, Germany*

Background: The progression from stable coronary artery disease to unstable acute coronary syndromes is associated with activation of cellular immune responses. Activation and differentiation of circulating lymphocytes is believed to represent part in this process. However, it remains controversial whether these mechanisms are cause or consequence of acute coronary syndromes.

Methods: To study the temporal relationship between progression of acute coronary syndromes and activation of cellular immune responses, we compared lymphocyte activation and differentiation towards Th1 or Th2 in patients without coronary artery disease (n= 7), with stable angina (n=14), with unstable angina (n=11) and with acute myocardial infarction (n=10). Lymphocyte activation was assessed using 3-color flow cytometry to quantify CD3+ cells producing IFN-γ (Th1), IL-4 (Th2) or both signature cytokines (Th0).
Results: In patients without coronary artery disease, 7.6±2.1% of peripheral CD3+ cells stained positive for IFN-γ. This proportion increased significantly in stable angina (13.9±1.3%, p<0.05) with a maximal expansion in patients with unstable angina (33.3±2.6%, p<0.0001 versus control and stable). In marked contrast in patients with acute myocardial infarction, the frequency of IFN-γ+/CD3+ cells declined to 7.3±1.6% (p<.0001 versus unstable). The frequency of IL-4+/CD3+ (p=0.64) or IFN-γ +/IL-4+/CD3+ (p=0.73) cells did not differ significantly between the different groups.
Conclusion: The present findings suggest that IFN-γ-producing Th1 cells, but not Th2 or Th0 cells, promote the progression of acute coronary syndromes. The transient nature of the expansion of circulating Th1 cells with an abrupt reduction if the instability progresses to acute myocardial infarction strongly supports the assumption of lymphocyte activation as a cause rather than a consequence of increasing plaque instability.



1054-97 Incidence of Underlying Coronary Artery Disease Among Patients Having Cocaine-Associated Chest Pain

Michael C. Kontos, Robert L. Jesse, James L. Tatum, Charlotte S. Roberts, Joseph P. Ornato. *MCV/VCU, Richmond, VA*

Patients who present to the Emergency Department (ED) with chest pain associated with cocaine use are an increasingly recognized problem. The incidence and predictors of underlying significant coronary disease (Sig CAD) in patients with and without MI has not been well described. **Methods:** Patients who underwent coronary angiography within 60 days of an ED evaluation for cocaine chest pain were included. Sig CAD was defined as ≥ 50% luminal stenosis of a cororary artery or one of its major branches. **Results:** From 6/94 to 3/00, 698 patients were evaluated for myocardial ischemia after cocaine use, of whom 84 subsequently underwent coronary angiography. Sig CAD was present in 40 (48%): 1 vessel in 24, 2 vessel in 8, 3 vessel in 5 and graft stenosis in 3. Sig CAD was present in 19/25 (76%) of the pts with acute myocardial infarction (AMI) compared to only 21/59 (36%; p=0.003) pts without AMI. Only AMI (48% vs 14%, p=<0.001), prior MI (25% vs 7%, p=0.02) and known CAD (prior MI or revascularization) (40% vs 11%, p=0.003) were associated with Sig CAD. There was no significant difference in the age (42±7 vs 42±9), gender (70% vs 73% male), or risk factors other than diabetes between those with and without Sig CAD. In the 54 pts without AMI only prior MI (25% vs 7%; p=0.02) and known CAD (40% vs 11; p=0.003) were predictive of Sig CAD; ischemic ECG changes were not (38% vs 23%; p=0.14). Only 12 pts (14%) of patients without AMI or known CAD had Sig CAD. **Conclusions:** Sig CAD is found in the majority of patients with cocaine-associated MI. In contrast, only a minority of patients with cocaine associated chest pain without MI have Sig CAD.

1054-98 Organized Thrombosis in Coronary Arteries of Young Sudden Cardiac Death Patients

Allard C. van der Wal, Rosa Henriques de Goveia, Anton E. Becker. *Cardiovascular Pathology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands*

Background. To get informed about plaque instability before the onset of death in young sudden coronary death patients. **Methods.** Eleven patients aged 35 years or younger who died instantly or within 6 hours after the onset of symptoms, and in whom coronary thrombus was found at autopsy, were enrolled in the study. The thrombosed artery segment was serially cut for histology (Haematoxylin and Eosin stain) and immunohistochemistry with antibodies reactive with smooth muscle cells (SMC) (anti- smooth muscle actin) and endothelial cells (anti- von Willebrand factor). **Results.** Atherosclerotic plaques underlying the thrombus showed deep ruptures in 2 cases, and surface erosions in 9 cases. Fresh thrombus was found in the culprit plaque of only 3 patients (including those with deep ruptures). The remaining 8 patients,all with eroded plaques, showed organized thrombus. In 4 of those, thrombus organisation consisted of ingrowth of actin positive SMC in the base of the thrombus (a few days old thrombus), in 4 patients there was extensive ingrowth of SMC, deposition of collagen and ingrowth of microvessels (more than a week old thrombus). **Conclusion.** Erosions are by far the dominant type of plaque complication in young patients who die due to coronary thrombosis. Presence of organizing thrombus in the majority of cases indicates plaque instability of at least days, up to more than a week before the onset of sudden death.

1054-99 Oxidative Stress and Redox Equillibrium in Patients With Coronary Vasospasm

Kunihisa Miwa, Toshinori Makita, Katuhisa Ishii, Nobuaki Okuda, Takaharu Saito, Chiharu Kishimoto, Hajime Nakamura, Junji Yodoi. *Kansai Electric Power Hospital, Osaka, Japan, Kyoto University, Kyoto, Japan*

Backgound. Increased oxidative stress has been implicated in the pathogenesis of coronary vasospasm. Thioredoxin is a redox-active protein which is known to be induced by oxidative stress and released from cells. The serum thioredoxin level may reflect systemic oxidative stress or redox equillibrium. In order to determine whether oxidative stress is actually accentuated in patients with coronary vasospasm, serum levels of both thioredoxin and antioxidant vitamin E were determined in patients with coronary spastic angina. **Methods.** The serum thioredoxin level was determined using enzyme-linked immunosorbent assay in 21 patients with active stage of coronary spastic angina with spontaneous anginal attacks at least twice a week (CSA), in 17 patients with inactive stage of coronary spastic angina with diagnosed coronary spasm but without angina for > 6 months (iCSA), in 26 control subjects without coronary artery disease (Control) and also in 26 patients with stable effort angina and a significant organic coronary stenosis but without rest angina (SEA). **Results.** The serum thioredoxin level (mean ± SD ng/ml) was significantly higher in CSA (64±44) than in iCSA (34±37), in Control (34±15) and also in SEA (37±16). In contrast, the serum alpha-tocopherol (mg/g lipids) level was significantly lower in CSA (2.8±0.7) than in Control (3.6±0.7). Current smoking was significantly more prevalent in CSA (76%) than in iCSA (24%), in Control (35%) and in SEA (23%). No significant correlation was found between the serum levels of thioredoxin and alpha-tocopherol. In 9 patients of CSA, the serum level of thioredoxin significantly decreased (93±41 to 41±35) and the serum level of alpha-tocopherol significantly increased (2.7±0.6 to 3.1±0.6) after a >3-month angina-free period under medication with calcium antagonists and smoking cessation education. **Conclusion.** Patients with coronary spastic angina in active stage had a higher serum thioredoxin level associated with a lower serum level of antioxidant vitamin E. Redox equillibrium appeared to be related to the disease activity of coronary vasospasm in these patients. Oxidative stress may play an important role in the genesis of coronary vasospasm.

1054-100 The Circumflex Artery: A Major Contributor in Nonq-Wave Myocardial Infarctions

Anil J. Mani, M. Karatepe, Zoran Lasic, E. Kreps, M. Collins, J. Moses, N. Coplan, I. Moussa. *Lenox Hill Heart and Vascular Institute, New York, NY*

Background: In patients presenting with an acute MI, the EKG has traditionally been utilized for treatment stratification. However, the EKG has significant drawbacks in evaluating events involving the left circumflex artery (LCX). This study was undertaken to evaluate the extent of contribution by the LCX artery in non Q-wave MI (NQWMI). **Methods:** Between January 1994 and December 1997, 404 consecutive patients (pts.) with NQWMI who underwent coronary angiography for risk stratification at our institution were identified. Demographic, in-hospital and angiographic data were collected. NQWMI was defined by presentation, EKG and a total CPK above normal with CPK-mb ≥ 5%. A large MI was defined as a peak CPK >5x normal. **Results:** The mean age of the study group was 65±12.3 years; 65% were male. The infarct related artery (IRA) was identifiable in 269 pts. (66.6%); 135 pts. had severe three vessel disease which prevented identification of the IRA. Total occlusions were present in 95/265 (35%) of IRA. The LCX artery accounted for 37.7% of all MI and 58.13% of all large MI with an identifiable IRA. Complete thrombotic occlusion with no collateral supply was significantly higher in the LCX artery as illustrated below:

IRA With Total Occlusion (n = 95)

	LAD(%)	LCX(%)	RCA(%)	LM(%)	SVG(%)
No Collateral(n=48)	25	64.6*	8.3	2.1	0
Collateral(n=47)	31.9	29.8	31.9	0	6.4

* p values: LCX vs. LAD (0.05),vs. RCA (0.0007), vs. SVG (0.03), vs. all other sites (0.0009) **Conclusions:** The LCX artery is a significant contributor to thrombotic vessel occlusions in NQWMI. These patients may benefit from immediate reperfusion therapy.

POSTER SESSION

1083 Stabile Ischemic Syndrome: Oxidative Stress Insulin Resistance and Inflammation

Monday, March 19, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 10:00 a.m.-11:00 a.m.

1083-75 Treatment With Folic Acid and Cobalamin Improves Coronary Endothelial Function in Hyperhomocysteinemic Patients With Symptomatic Coronary Artery Disease

Frank F. Willems, Wim RM Aengevaeren, Godfried HJ Boers, Henk J Blom, Freek WA Verheugt. *university medical center, nijmegen, The Netherlands, Rijnstate hospital, arnhem, The Netherlands*

Background: Hyperhomocysteinemia is an independant risk factor for coronary artery disease. It is unclear whether lowering homocysteine(HCY)with folic acid and cobalamine improves coronary endothelial function in patients with hyperhomocysteinemia and coronary artery disease.Aim of this study was to evaluate the effect of folic acid and cobalamine on coronary endothelial function in patients with symptomatic coronary artery disease. **Methods:** 17 patients sheduled for elective PTCA with HCY levels above 16 umol/l were randomised for treatment with folic acid 5 mg and cobalamine daily or placebo. Coronary endothelial function was evaluated in a non-PTCA vessel using acethylcholine infusion in an dosage of 10-8M, 10-7M, 10-6M and nitroglycerin 200ug.Each infusion was followed by coronary angiography. After 6 months of treatment a second procedure was performed using the same method. Endpoints were the mean changes in minimal obstruction diameter(MOD) and mean segment diameter(MSD)of the investigated coronary vessel as compared to the initial procedure. **Results:** Mean HCY level was 18,2umol/l (SD 2,34).The mean difference in MOD(%) before versus after treatment with folic acid and cobalamin is 103.6% compared to 87.1% in the placebo treated group ($p<0.05$). The mean difference in MSD (%) before versus after treatment with folic acid and cobalamin is 106.6% compared to 90.9% in the placebo treated group ($p<0.05$). **Conclusion:** This is the first randomised placebo controlled intervention study evaluating coronary endothelial function in hyperhomocysteinemic patients with symptomatic coronary artery disease. Our results suggest improvement of coronary endothelial function following treatment with folic acid and cobalamine

1083-76 Evidence of Oxidative Stress in Patients With Angina and Normal Coronary Arteries: Role of Statins and Ace-Inhibitors

Carmine Pizzi, Grazia Maria Costa,Barbara Bresciani, Milena Gentile, Carlo Tumscitz, Bugiardini Raffaele. *Dep cardiology Imola Hospital University of Bologna, Bologna, Italy*

Background. It is well known that the endothelial dysfunction plays a key role in the pathophysiology of the angina with normal coronary angiograms. The endothelial dysfunction is associated with increased oxidative stress (OS) and loss of nitric oxide bioavailability. Aim of study was to evaluate the influence of the therapy with statins and ACE-I on OS production in these pts. **Methods.** We studied 40 normocholesterolemic pts with effort angina (positive exercise stress testing and reversible reperfusion defects). In order to evaluate OS we measured (T1):plasma levels of malondialdhehyde (MDA), a marker of lipid peroxidation, by high pressure liquid chromatography (HPLC); superoxide dismutase (SOD) and CoQ10. 20 pts (G1) were treated with atorvastatin (40 mg/day)and ramipril (5 mg twice daily) for 6 months in addition to standard antiischemic treatment and 20 pts (G2) received only standard antiischemic treatment. After 6 months of therapy(T2) MDA, SOD and CoQ10 were measured. Changes in OS were correlated with clinical response. **Results.** Baseline characteristics (age, gender, risk factors of coronary artery disease) were similar in the 2 groups. At T1 MDA, SOD and CoQ10 showed no differences in G1 vs G2 (MDA:2.5+/-0.8 vs 2.4+/-0.9 nmol/ml; SOD:188+/-47 vs 180+/-51 U/mg Hb; CoQ10 1+/-0.2 vs 0.9 +/- 0.3 mg/dl). At T2 MDA was significantly reduced in G1 vs G2 (1.2+/-0.4 vs 2.3+/-1 nmol/ml; $p<0.001$). No changes were demonstrated in SOD in G1 vs G2(179+/-52 vs 176+/-62 U/mg Hb). CoQ10 was improved in G1 vs G2 (1.2+/-0.2 vs 0.7+/-0.2 mg/dl; $p<0.001$).At T2 in exercise stress test there were a significant increase in the exercise time and maximal work capacity and a significant decrease in the maximum ST segment depression in G1, no myocardial perfusion assessed by defect tallium tomography (SPECT) in 16 pts of G1 and only 3 pts of G2. **Conclusion.** Our data support the hypothesis that oxygen free radicals production may be an important role in microvascular endothelial dysfunction. Administration of antioxidant drugs which reverse endothelium dependent dysfunction may be useful in pts with angina and normal coronary angiograms, independently of plasma total cholesterol levels.

1083-77 Effects of Insulin Resistance and Thiazolidinedione on Effort-Induced Angina Pectoris With Type-2 Diabetes Mellitus

Tatsuaki Murakami, Masateru Ohnaka. *Fukui Cardiovascular Center, Fukui, Japan*

Background: Insulin resistance is thought to be highly involved in atherothrombogenic processes and effects of an insulin sensitizer on clinical manifestation of ischemic heart disease have marked attention, but few investigations evaluated effects of thiazolidinedione, and an insulin sensitizer, on ischemic heart disease. This study investigated whether insulin resistance and its reversal by thiazolidinedione have impacts upon clinical manifestations of effort-induced angina pectoris (EA). **Methods:** Type-2 diabetic patients (n=22) with EA and ischemic change on treadmill exercise test were enrolled into this study of thiazolidinedione, and randomized where they received troglitazone for 4 months (T-group, n=11) or they were followed without troglitazone (C-group). At baseline and at 4 months after medication, we assessed changes of exercise tolerance (appearance time of ischemic ST segment change) and noninvasively measured the reactive changes in lumen diameter of right brachial artery following transient occlusion for 5 minutes (FMD; flow-mediated endothelium-dependent vasodilation), and after sublingual administration of (300microgram) glyceril trinitrate (TNG; endothelium-independent vasodilation). **Results:** Exercise time (minutes) were significantly extended after medication in T-group ($p<0.01$) but not in C-group. HOMA index (product of fasting glucose and fasting insulin/405) and FMD (%) was improved after medication in T-group ($p<0.01$) but not in C-group. TNG remained unchanged in both groups. Extension of exercise time was correlated to improvement of FMD (Extension of exercise time (y) vs. improvement of FMD (x); $y=0.72+0.23x$, $r= 0.79$, $p=0.02$; and improvement of HOMAindex (x); $y=0.91+1.36x$, $r= 0.62$, $p=0.04$). **Conclusion:** These findings suggest that troglitazone reverses exercise intolerance partly related to endothelial dysfunction and insulin resistance in patients with effort-induced angina pectoris.

	Baseline T	Follow-up T	Baseline C	Follow-up C
Exercise Time	4.9±1.0	6.3±1.4	5.1±1.0	5.3±1.4
FMD	4.0±1.6	6.7±3.0	4.2±2.6	4.4±2.0
HOMA	2.6±1.4	2.1±1.1	2.5±1.2	2.5±1.2

1083-78 Effect of Cholesterol Synthase Inhibitor Treatment on Interleukin-6 and CRP in Patients After Myocardial Infarction

Stephan R. Holmer, Christian Hengstenberg, Hannelore Loewel, Susanne Engel, Wolfgang Koenig, Guenter A. J. Riegger, Heribert Schunkert. *University of Regensburg Klinik Innere Med. II, Regensburg, Germany, GSF- Institute of Epidemiology, Munich, Germany*

Background: Levels of cytokines (e.g. interleukin-6,IL6) and acute phase proteins (e.g. C-reactive protein,CRP) may indicate inflammatory activity in coronary lesions in patients with coronary artery disease and have been associated with prognosis. Chronic medication with CSE-inhibitors (statins) improves the prognosis of such patients. It was suggested that this treatment may modulate the inflammatory process.
Methods: We tested in stable patients with previous myocardial infarction (MI) whether IL6 and CRP levels are modulated by chronic statin intake. Patients form the MONICA MI-register, Augsburg, (n=642; 557 men) were examined 1-10 years (mean 5.6 years) after MI including a standardized interview (intake of prescribed medication), anthropometry, ECG, echocardiography and blood tests (e.g. IL6 high sensitive ELISA). None of the patients had signs of acute coronary syndrome.
Results: Of all MI patients, 31% were on statin treatment. Patients with statins showed significantly lower IL6 levels compared to those without lipid lowering drugs (2.2±0.1 pg/mL vs. 2.8±0.1; $p<0.0001$). This was most evident in men (2.1±0.1 vs. 2.8±0.1; $p<0.0001$). Similarly, CRP was lower in patients on statins (2.3±0.2 mg/L vs. 3.1±0.1; $p<0.0001$). Neither IL6 nor CRP levles were related to cholesterol levels. The association of statin treatment with IL6 and CRP levels was also highly significant in multivariate regression models that included age, body mass index, left ventricular function (EF) and cholesterol level as covariates ($p=0.004$ and 0.017, resp.). In the small number of women with MI no such association of IL6 or CRP levels with statin treatment was observed. Other medication such as ACE-inhibitors, beta-blockers, or vasodilators had no apparent effect on IL6 or CRP levels in this population.
Conclusion: In this observational study, statin therapy is strongly and independently associated with lower IL6 and CRP levels in male patients after MI. This further supports the concept that statin therapy attenuates the inflammatory process in atherosclerotic patients independently of its cholesterol lowering effect.

POSTER SESSION

1084 Advances in Cardiopulmonary Resuscitation

Monday, March 19, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 10:00 a.m.-11:00 a.m.

1084-79 Early Defibrillation Through First Responders Doubles Sudden Cardiac Arrest Survival in an Italian Community

Alessandro Capucci, Daniela Aschieri, Massimo F. Piepoli, Efi Iconomu, Maurizio Arvedi. *cardiology department, Piacenza, Italy*

Background. The concept that non medical individuals must be allowed to perform early defibrillation has been largely endorsed. To improve out-of-hospital survival we developed the Piacenza Progetto Vita project i.e. the first European experience of public access early defibrillation. **Methods and Results.** Thirty-three semi-automatic external defibrillators (Heartstart FR) were placed in this Italian city (266.531 including the surrounding region): 15 fixed places, 12 ambulances (laic personnel), 12 policemen cars. One thousand and twenty-five laic volunteers were trained for defibrillation. The volunteers are activated by the Emergency Medical System ("Blue Code" call) to intervene in all cases of suspected sudden death. During the first year 197 sudden deaths occurred in this area. During this time 198 "Blue Codes" were dispatched: in only 95 of such cases a true sudden death (48%) was found. The defibrillator was applied by volunteers in 63 cases: 36 asystole, 3 pulse-less electrical activity, 4 bradiarrhythmias, 1 supraventricular

tachycardia, 3 sinus rhythm, 16 "shockable rhythm". Seven patients were successfully cardioverted and discharged alive. One patient died after 15 days. Survival rate on "shockable" rhythm was 43.7% in laic responders system vs. 16.6% in the medical staff aid ($p< 0.05$). Among survivals the proportion having unfavourable neurologic function at hospital discharge decreased from 25% to 14%. In 106 "blue codes" the volunteers intervened before the medical staff (53%) (mean intervention time: 5.30 min + 0.40 min vs. 6.50 + 1 min, $p<0.05$). **Conclusions.** Preliminary experience of out-of-hospital early defibrillation by non-medical volunteers presents encouraging results even if the "3-minute response time" (optimal call-to-shock time) was not yet reached.

	Emergency Medical System	Laic Volunteers	p value
First at the scene	34%	53%	
Shockable Rhythm at the arrive (n° cases)	24	16	
Discharged alive (n° pts)	4/24 (16.6%)	7/16 (43.7%)	p<0.05
Neurologic lesions in pts alive	1/4 (25%)	1/7 (14%)	
Intervention time (min)	6.50+1.0	5.30+0.40	p<0.05

1084-80 Different Basic Life Support Compression to Ventilation Ratios: Effect on 24-Hour Neurologically Intact Survival

Karl B. Kern, Robert A. Berg, Ronald W. Hilwig, Arthur B. Sanders, Gordon A. Ewy.
University of Arizona, Tucson, AZ

Background: The recently published Guidelines 2000 for CPR and ECC suggests that "adult cardiac arrest (CA) victims are more likely to be saved if a higher number of chest compressions (CC) are delivered during CPR, even if victims receive fewer ventilations" (V). This study prospectively evaluated four different BLS CC:V ratios for the proportion of resuscitation time with CC-generated circulation and 24 hr neurologically intact survival. **Methods:** Forty swine (25-35 Kg) were subjected to 3 min of untreated VF then randomized to 1 of 4 different CC:V ratios including 15:2 (standard BLS), 50:5, 100:2, and CC-only BLS for 12 min. To mimic real life out-of-hospital resuscitation results, CPP was kept at 12-15 mmHg and previously documented pauses for lay persons to deliver ventilations were incorporated into the protocol (i.e 15 sec to deliver 2 mouth-to-mouth ventilations). Aortic and RA pressures, end-tidal CO2, ECG, and exhaled ventilatory volumes were recorded throughout. Intensive care was provided for 2-3 hrs and neurological evaluations were performed on all 24-hr survivors. **Results:** BLS at 15:2 resulted in only 42% of the resuscitation period with CC-generated circulation. 50:5 produced circulation 58% of time, 100:2 for 83%, and CC-only for 93%. Standard 15:2 produced 0/10 neurologically intact 24-hr survivors, 50:5 had 1/10, 100:2 had 0/10, and CC-only BLS had 3/10 (1/30 vs 3/10; p=0.042 via Fisher's Exact Testing). **Conclusion:** CC-only BLS results in more compression-generated circulation time and better 24-hr neurologically intact survival than the other CC:V ratios tested, including the currently recommended BLS with a 15:2 ratio.

1084-81 Postresuscitation Care in Survivors With Acute Coronary Syndrome Complicated by Out-of-Hospital Cardiac Arrest

Ken Nagao, Katsuo Kanmatsuse, Kazuyoshi Satou, Ikuyoshi Watanabe, Ken Arima, Sumito Oguchi, Satoru Kikuchi, Kimio Kikushima, Sigemasa Tani, Takeo Anazawa, Takashi Miyamoto. *Department of Emergency & Critical Care Medicine, Nihon University School of Medicine, Tokyo, Japan, Department of Cardiology, Nihon University School of Medicine, Tokyo, Japan*

Background : Almost one-half of postresuscitation syndrome deaths that occur take place within 24 hours of the event caused by microcirculatory dysfunction from the multifocal hypoxia. There are no convincing clinical data to evaluate the stress response hormones and coagulative fibrinolytic parameters in patients with acute coronary syndrome (ACS) complicated by out-of hospital cardiac arrest. **Methods:** A total of 252 patients whose ACS-related artery could be identified by emergency coronary angiography and whose blood test before administration of drugs could be obtained were chosen for this study. The stress response hormones and coagulative fibrinolyytic parameters of 55patients with ACS complicated by out-of-hospital cardiac arrest were compared with those from 197 patients with ACS without this complication.

Results

*P<0.05	cardiac arrest	without cardiac arrest
Dopamine *(pg/ml)	131	58
Noradrenaline *(pg/ml)	1843	913
Adrenaline *(pg/ml)	2096	280
Angiotensin II *(pg/ml)	47	9
Brain natriuretic peptide (pg/ml)	127	163
von Willebrand factor (%)	257	253
Free tissue factor pathway inhibitor (ng/ml)	46	56
Prothrombin fragment 1+2 *(n mol/l)	3.5	1.0
Antithrombin III (%) 85 86	85	86
Trombomodulin (Fu/ml)	3.4	3.0
Activated protein C (%)	68	86
t PA PAI-I complex	37	15
α2-PI complex	15	9
FDP *(μg/ml)	26	7
D-dimer *(μg/ml)	6.3	1.9

Conclusions. Prominant increases in the levels of circulating vasocontraction hormones and systemic thrombus formation were observed in patients with ACS complicated by out-of-hospital cardiac arrest. It was suggested that the managements of hypervasocontraction and hypercoagulopathy in survivors with ACS complicated by out-of-hospital cardiac arrest are needed for prevention of postresuscitation syndrome.

1084-82 Utilization of the Emergency Medical System Among Patients With Myocardial Infarction in the Reperfusion Era: Results From The NRMI 2

John G. Canto, Rob Zalenski, Joseph P. Ornato, William J. Rogers, Catarina I. Kiefe, David Magid, Michael Shlipak, Paul Frederick, Costas G. Lambrew, Hal V. Barron.
university of Alabama at Birmingham, Birmingham, AL

Background. National practice guidelines strongly recommend that patients with symptoms consistent with an acute myocardial infarction (MI) activate the 911 Emergency Medical Systems (EMS). We examined the contemporary utilization of EMS in the US, and ascertained the factors which may influence their use. **Methods.** From April 1994 to March 1998, the NRMI 2 has enrolled 772,586 patients. We excluded patients who presented in cardiogenic shock, >6 hours from symptom onset to hospital arrival, or who were transferred-in. We then compared the baseline characteristics and initial management for patients presenting by ambulance versus self-transport.

Results

	Ambulance	Self-Transport
N	175,517	153,365
%	53.4	46.6
Mean Age, years	68.1	63.7
Non-White, %	10.5	11.0
Men, %	60.0	69.0
HMO, %	11.2	11.8
Prior MI, %	27.8	24.2
Prior heart failure, %	15.1	8.2
Sx Onset to hospital arrival, min	90.0	102.0
Chest pain, %	78.5	89.9
Pre-hospital ECG and EMS	6.2	0.0
Mean time to 1st ECG, min	13.7	15.0
Mean door-thrombolytic, min	54.7	66.9
Mean door-to balloon, min	141.7	173.0

P value < 0.001 for all comparisons. **Conclusion.** Only 1 of every 2 patients with MI was transported to the hospital by ambulance. Use of the EMS was associated with significantly faster receipt of acute reperfusion therapies. Wider use of EMS for patients with suspected MI may offer considerable opportunity for improvement in public health.

1084-83 Open Chest Defibrillation: Biphasic Versus Monophasic Waveform Shocks

Yi Zhang, Ray Davies, William J. Coddington, Janice Jones, Richard E. Kerber.
University of Iowa, Iowa City, IA

Background: Transthoracic biphasic waveform shocks require less energy to terminate ventricular fibrillation (VF) compared to monophasic shocks. However, the effectiveness of biphasic shocks for intraoperative open chest epicardial defibrillation has not been established. Our purpose was to compare biphasic vs. monophasic shocks for open chest defibrillation, using a porcine model. **Methods:** Twenty-five adult swine (15-25kg) underwent a midline sternotomy. VF was electrically induced. After 15 seconds VF, each pig in Group 1 (n=16) received in random order damped sinusoidal monophasic shocks and truncated exponential biphasic shocks (3 msec positive and 3 msec negative) at 8 energy levels (2J, 3J, 5J, 7J, 10J, 20J, 30J and 50J) from large (44 cm) hand-held epicardial paddle electrodes. Pigs in Group 2 (n=9) received similar shocks from small paddle electrodes (16 cm2). Four shocks at each energy level were delivered to construct energy vs. success curves. **Results:** There was no significant difference in shock success between damped sinusoidal monophasic and biphasic waveform shocks at any energy level in Group 1 (large electrodes). In Group 2 (small electrodes), swine receiving biphasic shocks demonstrated a significantly higher shock success than those receiving monophasic shocks at 7J (<0.05), and there was a trend (p=0.06) in favor of biphasic shocks at 10J and 20J. **Conclusion:** With small paddle electrodes, biphasic waveform shocks demonstrated a higher shock success rate compared to monophasic waveform shocks at mid-range energy levels. With large paddle electrodes, biphasic and monophasic shocks were equally effective. Shocks given from small paddle electrodes may result in an inhomogeneous electrical field, allowing the superiority of the biphasic waveform to be evident. % Success Comparison. Mean +/- SEE, *p<0.05 vs. monophasic in small electrode group

		2 J	3 J	5 J	7 J	10 J	20 J	30 J	50 J
Large Electrodes	Biphasic	23+/-10	45+/-11	66+/-10	89+/-5	92+/-4	78+/-7	86+/-5	87+/-6
	Monophasic	25+/-9	51+/-9	72+/-9	76+/-10	89+/-6	86+/-5	83+/-6	88+/-7
Small Electrodes	Biphasic	10+/-5	30+/-11	61+/-11	75+/-6*	78+/-7	92+/-5	96+/-4	92+/-4
	Monophasic	2+/-2	5+/-3	30+/-11	46+/-7	37+/-8	67+/-8	79+/-8	81+/-7

POSTER SESSION

1085 Blood Risk Markers in Acute Coronary Syndromes

Monday, March 19, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 10:00 a.m.-11:00 a.m.

1085-84 C-Reactive Protein and ST Segment Monitoring With Continuous 12-Lead Electrocardiogram in Patients With Unstable Angina

Alexander Stefanidis, Michael Zairis, Stavros Manousakis, Evangelos Tsanis, Thomas Matsikas, Maria Thoma, John Hadjissavas, Apostolos Papantonakos, Stelios Handanis, Kostas Katsaros, Spyros Argyrakis, Stefanos Foussas. *Cardiology Department, Tzanio Hospital, Piraeus, Greece*

Background: ST segment monitoring by the continuous 12-lead electrocardiogram (ECG) has been a useful tool for the quantification of recurrent ischemia in patients (pts) with unstable angina (UA). Additionally, high levels of C-reactive protein (CRP) have been associated with an unfavorable outcome in these pts. However, the possible relation of CRP levels with the incidence and severity of recurrent ischemia in pts with primary UA by the use of continuous ECG monitoring was not thoroughly investigated. The aim of this study was to evaluate the possible association of plasma levels of CRP to recurrent ischemia detected by continuous 12-leads ST monitoring. **Methods:** A total of 111 pts with Brawnwald IIIB UA underwent continuous ST segment monitoring for 48 hours with a computer-assisted 12-lead ECG-ischemia monitoring device. An ST ischemic episode was defined as a transient ST-segment depression or elevation in any lead of at least 0.10 mV compared with the reference ECG, lasting for at least 1 min. Vein blood samples for plasma CRP values determination were obtained on admission. Pts were classified into three groups A, B, and C according to the tertiles of plasma CRP values. [Mean value of plasma CRP: Group A (40 pts)=0.56±0.15, Group B (37 pts)=1.78±0.43, Group C (34 pts)=3.16±0.64 mg/dl]. **Results:** Twenty-six out of 111(23.4%) patients had at least one ST ischemic episode (6, 8 and 12 pts for the A, B, and C groups respectively, p=0.11). However, the group C pts had significantly more ischemic episodes per patient than the group B (3.75±1.1 vs. 2.50±1.1, p=0.03), and than the group A (3.75±1.1 vs. 1.67±0.5, p=0.001) pts. Additionally, the total duration of ST ischemic episodes was significantly higher in the group C than the group B (56.41±16.27 min vs. 35.12±23.01 min, p=0.04), and than the group A (56.41±16.27 min vs. 19.50±11.04 min, p=0.001). **Conclusions:** Plasma levels of CRP could predict the total recurrent ischemic burden in pts with UA. Thus, plasma CRP levels on hospital admission may serve as an affordable and widely available marker for the detection of pts with silent or clinical obvious recurrent myocardial ischemia. These pts could benefit from more aggressive pharmaceutical or invasive treatment.

1085-85 Inflammatory Markers in Patients With Acute Coronary Syndromes Supressed by Alphatocopherol: Evidence From a Randomized Controlled Trial

R T. Murphy, J B. Foley, N McCarroll, K S. Lee, P Crean, M J. Walsh. *Department of Cardiology, St James's Hospital, Dublin, Ireland*

Background: The acute phase proteins C-Reactive Protein (CRP) and Interleukin-6 (IL-6) have been shown to be elevated in Acute Coronary Syndromes (ACS) and are associated with an adverse prognosis. Cell Adhesion Molecules are transmembrane glycoproteins which mediate leukocyte/endothelial binding, and are elevated in ACS. Alphatocopherol has extensive antiinflammatory properties. In a double blind placebo controlled trial, we set out to determine the antiinflammatory effects of alphatocopherol on patients presenting with ACS. **Methods:** 110 patients presenting with ACS were randomized to alphatocopherol 400 i.u. or matching placebo daily for 6 months. Serum samples were drawn at presentation 2, 4, and 6 months. CRP was measured by high sensitivity nephelemetry assay. IL-6 and the adhesion molecules soluble Vascular Cell Adhesion Molecule-1(sVCAM-1), soluble Intercellular Adhesion Molecule-1(sICAM-1), soluble E-Selectin, soluble P-Selectin, were measured using enzyme linked immunosorbent assay (R+D,UK) and alphatocopherol and lipid levels measured by high performance liquid chromatography. A subset of patients underwent flow cytometric analysis of monocyte adhesion molecule ligand expression. **Results:** Alphatocpherol/total lipid ratio rose in the treated group by 190% and fell in the placebo group by 40%. Mean CRP levels fell in the alphatocopherol group (from 21.8±7.1 to 5.2±0.6 mg/L, p<0.003), whereas CRP levels in the placebo group remained unchanged (17.4±4.4 vs 10.2±8.2 mg/L, p=0.2). Mean IL-6 levels fell in the alphatocopherol group (from 19.5±3.6 to 5.6±0.4 pg/ml, p<0.008) whereas levels of IL-6 fell nonsignificantly in the placebo group (17.9± 2.7 vs 7.7±1.9 pg/ml, p=0.2). There was no significant difference in soluble Cell Adhesion Molecule levels between treatment groups. Flow cytometric analysis failed to show inhibition of the monocyte adhesion molecule ligands Mac-1 and VLA-4. **Conclusion:** In patients with ACS, alphatocopherol suppressed the expression of CRP and IL-6. These observations may be of clinical relevance and justify assessment in a larger clinical trial.

1085-86 Hyperaggregability Persists in Spite of Blood Coagulability and Impaired Fibrinolysis After Stabilization in Patients With Unstable Angina

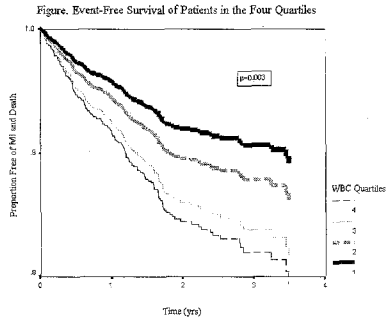
Shinzo Miyamoto, Hisao Ogawa, Hirofumi Soejima, Keiji Takazoe, Hideki Shimomura, Ichiro Kajiwara. *Department of Cardiovascular Medicine, Kumamoto University, Kumamoto City, Japan*

Background: Recently, platelet aggregometer using a laser-light scattering is capable of monitoring the increase in size of small-sized platelet aggregates (diameter 9-25μm) which can not be detected with the conventional methods. Small-sized platelet aggregates ultimately develop into medium and large-sized platelet aggregates as platelet aggregation proceeds. **Methods:** We examined platelet aggregability, especially small-sized platelet aggregates, plasma tissue factor (TF) antigen levels, and plasma plasminogen activator inhibitor (PAI) activity levels on admission and after treatment in 22 patients with UA. We also compared the results with data in 19 patients with stable exertional angina (SEA) and in 17 patients with chest pain syndrome (CPS). **Results:** The number of small-sized platelet aggregates increased significantly in the UA group [4.6+/-0.8X10exp(4) (V)] than in the SEA [3.6+/-0.9X10exp(3) (V), p<0.001] and CPS groups [2.0+/-0.7X10exp(3) (V), p<0.001]. In the UA group, the number of small-sized platelet aggregates after 2 weeks of treatment decreased significantly, but was still significantly higher compared with the SEA and CPS groups (p<0.01). The plasma TF antigen levels and the plasma PAI activity levels were higher in the UA group [TF:309+/-28 (pg/ml), PAI:12.3+/-2.2 (IU/ml)] than in the SEA [TF:215+/-11 (pg/ml), PAI:3.3+/-0.8 (IU/ml), p<0.01] and CPS groups [TF:191+/-16 (pg/ml), PAI:3.4+/-1.3 (IU/ml), p<0.01]. Each level decreased after 2 weeks of treatment in the UA group (p<0.01). There were significant correlations among 3 markers. **Conclusions:** We demonstrated that small-sized platelet aggregates, plasma TF antigen levels, and plasma PAI activity levels increased simultaneously in the UA group. Although the blood coagulation and fibrinolysis markers decreased after clinical stabilization, platelet hyperaggregability persisted. These results confirm that continuous antiplatelet therapy is essential after stabilization of unstable angina.

1085-87 The Leukocyte Count Predicts Future Cardiovascular Events in Patients With a Past Myocardial Infarction

Raef H. Hajj-Ali, Wojciech Zareba, Rana Z. Ezzeddine, Arthur J. Moss. *North Shore University Hospital, Manhasset, NY, University of Rochester, Rochester, NY*

Background: Increasing evidence is accumulating implicating inflammation as a risk factor for coronary artery disease. We thought to determine whether the leukocyte count is an independent predictor of future cardiovascular events in patients with a past myocardial infarction.
Methods: The study population consisted of 1,294 patients in whom a leukocyte count was obtained 6 months after the index MI. Cardiac events were defined as reinfarction or death. The study population was divided into four quartiles, Q1, Q2, Q3 and Q4 based on the leukocyte count.
Results: Over a mean follow-up period of 25 months from the leukocyte count measurement, 163 patients had cardiac events: 8.7%, 10.9%, 14.0%, and 16.7%, in Q1, Q2, Q3, and Q4 respectively (p=0.01). After adjusting for potential confounding factors, Cox proportional hazard analysis revealed a higher leukocyte count to be an independent predictor of cardiac events (Figure)



(Hazard Ratio: 1.3 per one quartile rise in leukocyte count; p=0.003; 95%CI [1.1-1.5])
Conclusion: The leukocyte count is an inexpensive and readily available independent predictor of future cardiovascular events in patients with a history of a myocardial infarction.

1085-88 Ability of the Human Heart Type-Fatty Acid Binding Protein to Predict Early Adverse Outcomes in Patients With Suspected Acute Coronary Syndrome in Emergency Room: A Multicenter Study

Tomoaki Nakata, Tohru Takahashi, Mamoro Hase, Hitoshi Oh-iwa, Akira Hashimoto, Kazuhiko Nagao, Takayuki Matsuki, Hiroshi Kobayashi, Kazufumi Tsuchihashi, Kazuaki Shimamoto. *Sapporo Medical University School of Medicine, Sapporo, Japan*

Background: Human heart type-fatty acid binding protein (H-FABP) has been demonstrated as a new marker of early myocardial injury in patients with acute myocardial infarction (AMI). However, the early prognostic value in acute coronary syndrome (ACS) has not been established. The present multicenter prospective study was designed to investigate the ability of H-FABP for predicting early clinical outcomes in patients with suspected ACS in emergency room by comparing with conventional serum markers.

Methods: We measured H-FABP, myoglobin (Mb), troponin T (TnT), and creatine kinase MB activity (CK-MB) in 133 patients with acute chest pain suggestive of ACS. The first biochemical data obtained at presentation to an emergency room was used to assess the ability to predict adverse outcomes that included emergent hospitalization, coronary angiography (CAG), ACS, AMI, and early coronary revascularization. **Results:** The first samples were obtained within 6 hours from onset (0-6 hrs data) in 74 (56%) patients. The diagnoses of ASC and AMI were established in 90 (68%) and 58 (44%) patients, respectively. H-FABP had the greatest sensitivities for identifying early adverse outcomes and the largest ROC areas for detecting AMI and ACS among the markers. **Conclusion:** H-FABP could have the greatest ability among biochemical markers to predict early adverse outcomes in patients presenting with suspected acute coronary syndrome in emergency room.

ROC area of each biochemical marker

	H-FABP	Mb	TnT	CK-MB
ACS(0-6hrs)	0.875	0.813	0.764	0.851
ACS(all)	0.800	0.756	0.776	0.739
AMI(0-6hrs)	0.876	0.837	0.792	0.839
AMI(all)	0.907	0.860	0.838	0.826

1085-89 Heart-Type Fatty Acid-Binding Protein Is More Useful Than Cardiac Troponin T and CK-MB Isoforms for Risk Stratification in Patients With Acute Coronary Syndrome Within 3 Hrs After Onset of Chest Pain

Junnichi Ishii, Masanori Nomura, Hiroyuki Naruse, Yoshihisa Mori, Toshikazu Ando, Hiroshi Kurokawa, Takeshi Kondo, Yoshihiko Watanabe, Hitoshi Hishida. *Fujita Health University, Toyoake, Japan*

We have previously reported that heart-type fatty acid-binding protein (FABP) is a more sensitive and specific marker than myoglobin for the early diagnosis of acute myocardial infarction (AMI). To evaluate the utility of serum FABP for early risk stratification in patients with acute coronary syndrome (ACS), we prospectively studied 195 consecutive patients (mean age +/- SD: 64 +/- 11 yrs) admitted to CCU for ACS within 6 hrs (4.3 +/- 2.2 hrs) after onset of chest pain. Serum levels of FABP were measured at admission, together with serum cardiac troponin T (TnT) and plasma CK-MB isoforms (MB iso). The cutoff values were as follows: FABP, 9 ng/mL; TnT, 0.10 ng/mL; MB iso, MB2 activity, 2.6 IU/L plus MB2/MB1, 1.7. **Results:** There were 114 patients with AMI and 81 with unstable angina pectoris (UAP). Twelve patients with UAP had cardiac events (1 death, 3 AMI and 8 UAP requiring intervention) within 48 hrs after admission. The 126 high-risk ACS patients were defined as AMI or UAP with cardiac events. The high-risk ACS patients had significantly ($p<0.0001$) higher levels of FABP (80.8 +/- 108.9 vs 5.9 +/- 4.6 ng/mL), TnT (1.38 +/- 2.52 vs 0.05 +/- 0.05 ng/mL), MB2 activity (36.2 +/- 69.0 vs 2.3 +/- 1.8 IU/L) and MB2/MB1 (3.0 +/- 2.0 vs 1.2 +/- 0.66) than patients without high-risk ACS. The sensitivity and predictive accuracy of FABP for the detection of the high-risk ACS in patients with ACS within 3 hrs after onset were higher than those of TnT ($p<0.0001$ and $p=0.02$) or MB iso ($p=0.0018$ and $p=0.03$) (Table). **Conclusion:** These findings suggest that FABP is a more useful marker than TnT and MB iso for early risk stratification in patients with ACS within 3 hrs after onset of chest pain.

***p<0.05 , **p<0.01 vs FABP.**

	Sensitivity			Specificity			Predictive accuracy		
Hrs after onset	FABP	TnT	MB iso	FABP	TnT	MB iso	FABP	TnT	MB iso
0 – 3	79% (42/53)	47%** (25/53)	57%** (30/53)	75% (21/28)	93% (26/28)	82% (23/28)	78% (63/81)	63%* (51/81)	65%* (53/81)
3 – 6	73% (53/73)	64%* (47/73)	68% (50/73)	88% (36/41)	98% (40/41)	98% (40/41)	78% (89/114)	76% (87/114)	79% (90/114)

POSTER SESSION

1086 Fibrinolytic Advances in the Treatment of Acute Myocardial Infarction

Monday, March 19, 2001; 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 10:00 a.m.-11:00 a.m.

1086-90 A Significant Infarct Related Stenosis After Successful Thrombolysis: Not Associated With Adverse Clinical Outcome but a Strong Predictor of Reocclusion

Peter C. Klevit, Marc A. Brouwer, Gerrit Veen, Johan Karreman, Freek W. A. Verheugt. *Heartcenter, University Medical Center, Nijmegen, The Netherlands, Free University Hospital, Amsterdam, The Netherlands*

Background: Routine angioplasty of a significant infarct related stenosis early after successful thrombolysis has not been proven superior to a conservative strategy with respect to reocclusion related events as mortality and reinfarction. However, in ~ 60% of patients reocclusion occurs without these events while left-ventricular recovery is precluded. This analysis addresses the importance of a significant stenosis regarding clinical events and reocclusion following an ischemia-guided revascularization strategy. **Methods:** In the first Antithrombotics in the Prevention of Reocclusion In COronary Thrombolysis (APRICOT) trial 248 patients had thrombolysis for suspected acute myocardial infarction with a patent infarct artery at angiography < 48 hours with 3 month follow-up angiography. QCA-analysis was possible in 240 patients: a > 60% stenosis was considered significant. An ischemia-guided revasculatization (revasc) strategy was followed. **Results:** A > 60% QCA stenosis was seen in 43% (103/240) of patients. Median clinical follow-up was 858 days (25th-75th percentile: 565-1293). Survival free from death or reinfarction (death/re-MI) was 85% in patients with a < 60% stenosis as compared to 82% in patients with a > 60% stenosis (p=ns). Including revasc, the rates were 70% and 66%(p=ns). At multivariate analysis a > 60% stenosis was not a predictor of death/re-MI or the combination of death/re-MI/revasc: odds ratios 1.17 (95% CI 0.58-2.38) and 1.18 (95% CI 0.67-2.08). Reocclusion was seen more often in patients with a > 60% stenosis: 41% (42/103) versus 18% (25/137) ($p<0.01$). Multivariate analysis identified a > 60% stenosis as an independent predictor of reocclusion: OR 2.91 (95% CI 1.60-5.29; $p<0.01$). **Conclusions:** Long-term clinical outcome following an ischemia-guided revascularization strategy after successful thrombolysis is excellent irrespective of the presence of a significant infarct related stenosis. However, a significant infarct related stenosis is associated with an increased risk of reocclusion, mainly occurring without death or clinical reinfarction. The effect of a routine invasive strategy in the prevention of reocclusion remains to be determined.

1086-91 Safety and Angiography Data of Amediplase, a New Fibrin Thrombolytic Agent, Given as a Single Bolus to Patients With Acute Myocardial Infarction: The 2K2 Dose Finding Trial

Frank Vermeer, Jurgen Pohl, Keith Oldroyd, Stefano Giannelli, Bernard Charbonnier. *University Hospital Maastricht, Maastricht, The Netherlands*

Background: Amediplase is a new thrombolytic agent with a potent fibrinolytic activity and high fibrin specificity. Its innovative structure results from conjugating two parts of the human plasminogen activators, the kringle 2 domain of t-PA (alteplase) and the catalytic chain of scu-PA (saruplase). **Methods:** This was an open-label, multicenter, randomized, dose finding study to evaluate the efficacy and safety of amediplase, given as single bolus in the dose range of 20 to 90 mg in patients with suspected acute myocardial infarction treated with heparin and aspirin within 6 hours from onset of symptoms. Efficacy was evaluated by measuring coronary artery patency (TIMI 3 flow grade) at 90 minutes angiography performed after amediplase administration. Rescue PTCA was performed in patients with TIMI 0-2 flow at 90 minutes. **Results.** 140 out of the 149 randomized patients were evaluable for angiographic data. TIMI 3 above 50% was achieved at ≥ 70mg amediplase doses. When doses were calculated adjusted to body weight, TIMI 3 >50% was achieved at ≥ 0.8mg/kg body weight. Mortality at 30 days was remarkably low, being 3.4% (5/149). Thirty-two serious adverse events were reported, mostly related to the myocardial infarction. Only one intracranial hemorrhage and one other fatal major bleed were reported. Pharmacokinetic analysis showed a plasma half-life value supporting single bolus dosing. **Conclusions.** 1) TIMI 3 flow at 90 minutes was obtained in more than 50% of the patients treated with doses ≥ 70mg corresponding to ≥ 0.8mg/kg body weight. 2) Amediplase has a good safety profile with a low incidence of serious bleeding complications. 3) Further investigations need to be performed to assess the optimal dose regimen for amediplase.

1086-92 Comparative Fibrinolytic Activity Profiles of the New Single-Bolus Thrombolytics Tenecteplase and Lanoteplase During Treatment of Patients With Acute Myocardial Infarction

Kamal A. Al Shwafi, Antoine de Meester, Bruno Pirenne, Jacques J. Col. *University of Louvain, Brussels, Belgium*

Background: New t-PA mutants with prolonged plasma half-life allowing a single-bolus administration have been tested. Tenecteplase (TNK-tPA) has a half-life of 20 minutes (min), lanoteplase (nPA) of 37 min. Efficacy and safty profiles of both agents were compared to that of the front-loaded t-PA, but no fibrinolytic activity (FA) assessment was performed. Therefore, a comparison of FA profiles of these agents is of importance to evaluate the differences in clinical outcome. **Methods:** Fibrinolytic activities of whole blood samples were assessed immediately after collection by measuring clot lysis onset time (LOT) using a bedside thrombolytic assessment system (TAS) before, 10, 60, 90, and 180 min after drug administration in 42 AMI patients, 19 were treated with 30-40 mg TNK-tPA, and 23 received 120 kU/kg nPA as a single-bolus. FA is non-detectable when LOT >1200 seconds (sec); the shorter LOT is, the more intense the FA. **Results:** Baseline LOT was >1200 sec in all patients. LOT was significantly shortened by the boluses of both agents, and was shorter after TNK-tPA than after nPA (median 111 vs 133 sec respectively). FA after both agents waned gradually, but it was much slower with nPA, the half-life of FA was 50 min for TNK-tPA and 69 min for nPA ($p<0.005$). FA 180 min after start of therapy was more intense with nPA than TNK-tPA, it was detected in 87% of patients given nPA compared to 59% received TNK-tPA ($p<0.001$). **Conclusion:** The more intense FA achieved immediately after the bolus of TNK-tPA could be translated to more rapid reperfusion rate, and the prolonged intense activity beyond 180 min after nPA could explain the increased rate of intracranial hemorrhage observed in the In TIME II trial. Thus characterizing the FA profiles of thrombolytic regimens might provide an insight in explaining the differences in efficacy and safty profiles of existing agents, and developing more desirable characteristics in future agents.

1086-93 Thrombolysis for Acute Myocardial Infarction in Patients Older Than 75 Years: Lack of Benefit for Hospital Mortality but Improvement of Longterm Mortality: Results of the MITRA- and MIR-Registries

Anselm K. Gitt, Ralf Zahn, Harm Wienbergen, Tobias Heer, Steffen Schneider, Martin Gottwik, Martin Gottwik, Jochen Senges, Rudolf Schiele. *Herzzentrum Ludwigshafen, Ludwigshafen, Germany*

Backgound: Meta-analysis of large randomized trials has shown that thrombolysis for acute myocardial ST-elevation infarction (AMI) reduces 35-day-mortality in patients (pts) ≥75 years by 1% which did not reach statistical significance. Recently published registry data even documented a lack of benefit for thrombolysis in AMI-pts ≥75 years. **Methods:** We analysed the prospective data of 6815 / 25194 (27%) unselected AMI-patients ≥75 years of MITRA (Maximal Individual Therapy of AMI Registry) and MIR (Myocardial Infarction Registry) to identify the impact of reperfusion therapy on hospital and longterm outcome (18 months) after AMI. **Results:** Only 2149 / 6815 AMI-pts ≥75 years (32%) did receive acute reperfusion therapy, 1782 (27%) thrombolysis, 367 (5%) primary PTCA. The main determinants of withholding reperfusion therapy in the elderly were increasing age per year (OR 0.90, CI 0.89-0.92), heart failure on admission (OR 0.65, CI 0.54-0.78) and heart rate >100/min (OR 0.66, CI 0.57-0.77). Hospital and longterm mortality were 29.5% / 34.1% in pts without reperfusion therapy, 25.4% / 19.6% in pts with thrombolysis and 16.3% / 14.5% in pts with primary PTCA as acute treatment for AMI. After correcting for baseline differences and presence of concomitant diseases thrombolysis for AMI did not influence hospital mortality but did influence longterm mortality (Table). Primary PTCA in AMI-pts ≥75 years significantly reduced even hospital mortality as well as longterm mortality (Table):

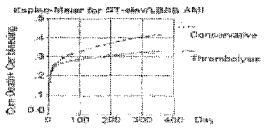
Multivariate Analysis	Hospital Mortality OR, 95% CI	18-Months-Mortality OR, 95% CI
Thrombolysis	0.95, 0.81-1.12	0.58, 0.39-0.88
Primary PTCA	0.39, 0.27-0.57	0.43, 0.20-0.93

Conclusions: Acute thrombolysis for AMI did not influence hospital mortality in pts ≥75 years, but was associated with a 42% lower longterm mortality. In comparison, primary PTCA for AMI was associated with a 61% lower hospital mortality and an additional 56% lower longterm mortality in pts ≥75 years.

1086-94 Thrombolysis Is Beneficial in Elderly Acute Myocardial Infarction Patients

Ulf Stenestrand, Lars Wallentin, the RIKS-HIA group. *Heart Center, University Hospital, Linkoping, Sweden, Dept of Cardiology, University Hospital, Uppsala, Sweden*

Background: Recent reports have stated that thrombolysis would not be beneficial in acute myocardial infarction (AMI) patients 75 years and older. We sought to investigate whether this was true in an unselected Swedish AMI population.
Methods: From the Swedish Register of Cardiac Intensive Care, which included every CCU admitted patient at 58 participating hospitals 1995-98, we studied 5,428 AMI patients >=75 y old admitted with ST-elevation or LBBB. Cox regression analysis was performed evaluating the effect of thrombolysis regarding the combined variable cerebral bleeding and one-year mortality taking into consideration 26 factors known to influence survival such as clinical background, medication, interventions and complications.
Results: There were 0.4% (9) mortal and 0.5% (12) cerebral bleedings in the 2,445 patients receiving thrombolysis. The combined endpoint of cerebral bleeding plus death of any cause within one year proved to have a significantly (p<0.001) lower incidence in the thrombolysis treated group 38.3% (699) compared to the conservative group 48.4% (1,145 of 2,983)). In Cox regression analysis adjusting for the 26 covariates thrombolysis treatment was associated with a risk reduction of 12% for the combined complications RR 0.88 (95% CI 0.79-0.97), p=0.011.
Conclusion: Even though increased incidence of severe bleeding complications in patients 75 years and older the total one-year mortality and cerebral bleedings endpoint is significantly lower in the thrombolysis treated group. Thus clearly indicating that thrombolysis is indicated even in elderly patients with ST-elevation or LBBB AMI.



1086-95 Weight-Based Dosing of Thrombolysis: How Well Do We Estimate Weight? How Often Would This Translate Into Errors With Administration of Thrombolytic Drugs? A Comparison of Single-Bolus TNK With t-PA in TIMI 10B

Christopher P. Cannon, Michael Gibson, Sabina A. Murphy, Frans Van de Werf, Carolyn H. McCabe. *Brigham and Women's Hospital, Boston, MA*

Weight-based dosing of thrombolytic drugs and heparin is recommended, notably for the new thrombolytic agent TNK, but obtaining an actual weight for a patient in the Emergency Department is difficult and often not done. Few data are available regarding the accuracy of estimated weight, or how often it would lead to a different dose of a thrombolytic drug. With weight-based dosing of TNK, dose increases with increments of 10 kg. For t-PA patients < 67 kg should receive a weight-based dose. **Methods:** We compared the estimated weight used in the Emergency Department vs. an actual weight obtained later in-hospital in 780 patients in the TIMI 10B. We then compared the accuracy of dosing between accelerated t-PA and single-bolus TNK in the TIMI 10B patients and 3253 patients in ASSENT I trials. **Results:** In TIMI 10B, estimated and actual weight correlated very well, R2=0.93 p<0.0001. Among TNK patients only 1 (0.4%) had estimated weight 10 kg under actual weight, and only 4 (1.7%) was the estimated weight higher than actual.(Total only 2.1% error in weight estimation that would change the dose for TNK). For the 290 t-PA patients, 6 (2.1%) were incorrectly estimated to weight <67 kg, and of these half received an incorrect weight-adjusted dose. In addition, 7 (2.4%) were incorrectly estimated to weight >=67 kg, and all 7 of them received a full 100 mg dose.(Total of 4.5% incorrect weight-adjusted dosing.) For TNK, in TIMI 10B and ASSENT I patients were randomized to receive a fixed dose of 30, 40 or 50 mg. Only 49/3730 (1.3%) of TNK patients received an incorrect dose. There was no difference in mortality or intracranial hemorrhage in TNK patients who received an incorrect dose. **Conclusion:** Errors in estimating weight are uncommon, especially those that would lead to a dose change. Dosing errors were extremely rare for TNK in the TIMI 10B and ASSENT I trials, and no adverse outcomes were seen among patients who received an incorrect dose - suggesting a broad safety profile for the new single-bolus agent TNK.

POSTER SESSION

1087 Myocardial Preservation: Experimental Insights

Monday, March 19, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 10:00 a.m.-11:00 a.m.

1087-96 Brain Natriuretic Peptide Mirrors Left Ventricular Remodelling Over 2 Months After First Myocardial Infarction

Jenifer Crilley, Martyn Farrer. *Sunderland Royal Hospital, Sunderland, United Kingdom*

Background: Brain natriuretic peptide (BNP) has been shown to be a strong predictor of mortality after myocardial infarction (MI). The mechanism may be linked to higher BNP levels being associated with adverse left ventricular (LV) remodelling. We investigated this in an unselected cohort of patients having their first MI, all of whom received thrombolysis. **Methods:** 133 patients who met the entry criteria of first MI and survival to 3 days had echocardiography to assess LV volumes and wall motion index (WMI-9 segment model) and samples taken for BNP assay at 3-7 days (early) and 2 months (late). Patients were followed for 1 year. A WMI cut-off of 1.2 was used to indicate LV dysfunction and BNP analysed according to %change in end-systolic volume index (ESVi) between the 2 studies. A multiple regression model was constructed to examine the influence of remodelling characteristics on BNP levels and 1 year mortality. Data is presented as mean (SEM); BNP in pg/ml. **Results:** Mortality was 7%. BNPearly was associated with 1 year cardiac mortality (cardiac death: 675 (135) pg/ml v alive: 365 (22) pg/ml). BNP levels and remodelling characteristics are seen in the table. Multiple regression modelling showed that the significant associations with BNPearly are WMIearly <1.2 (p<0.001) and ESVi dilatation (p<0.028) and with BNPlate, ESVi dilatation (p<0.001) and WMIearly <1.2 (p<0.006). **Conclusions:** BNP is a marker of early post-MI remodelling and initially reflects the magnitude of the infarct zone but later mirrors progressive LV dilatation. The ability of BNP to predict mortality after MI is linked to its association with adverse LV remodelling characteristics.

	WMI <1.2 (early)	WMI > 1.2 (early)
BNP (early)	579 (63)*	329 (21)*
BNP (late)	517 (65)**	345 (26)**

	>10% rise in ESVi	no change	>10% fall in ESVi
BNP (early)	454 (46)#	334 (34)#	326 (34)#
BNP (late)	498 (48)$	338 (44)$	269 (28)$

*p=0.001; **p=0.021 by unpaired t-test and #p=0.034; $p=0.001 by ANOVA

1087-97 Aminophylline Improves Regional Function in Chronic Ischemic Cardiomyopathy: Further Evidence That Adenosine Contributes Towards Functional Downregulation

Elizabeth Le, Howard Leong-Poi, Se-Joong Rim, Tadamichi Sakuma, Nicholas Fisher, Sanjiv Kaul. *University of Virginia, Charlottesville, VA*

Background: The neurohumoral mechanisms of reduced left ventricular function in chronic ischemic cardiomyopathy are not well understood. One possible regulator is adenosine, which has been shown to exhibit cardioprotective mechanisms via negative inrotropy. We have previously shown that infusion of 8-cyclopentyl 1,3 dipropylxanthine, a selective A1-adenosine receptor blocker, in the canine model of chronic ischemia resulted in improvement in percent wall thickening (%WT) but had no effect in transmural blood flow. We therefore hypothesized that infusion of aminophylline, a nonselective and competitive inhibitor of adenosine, would similarly result in improvement of myocardial function.
Methods: We placed ameroid constrictors on the proximal LAD and LCx arteries and their major branches in 7 adult mongrel dogs, which resulted in severe left ventricular dysfunction 4-7 weeks later. Closed-chest short-axis images at the low mid-papillary level were obtained before and immediately after injection of aminophylline (4mg/Kg) using 2-D echocardiography. Heart rate and mean blood pressures were also monitored during the experiments. % WT and wall thickness in the LAD and LCx regions and end-systolic and end-diastolic areas were calculated using custom designed software.
Results: Aminophylline increased heart rate significantly from 92±7 to 114±11 beats/minute (p<0.05) but did not affect mean aortic pressure (114±9 Versus 107±11 mm Hg). % WT and wall thickness were equally reduced in the LAD and LCx beds prior to aminophylline infusion. After infusion of aminophylline, % WT increased from 7.2±2.1 to 18.4±2.5% in the LAD region (p=0.001) and from 9.3±2.3 to 21.74±2.0% in the LCx region (p=0.006). Wall thickness during diastole did not alter significantly in either region.

Conclusion: These results indicate that adenosine plays a significant role in the down-regulation of myocardial function in chronic ischemia and probably serves as a cardioprotectant, especially during periods of repetitive stress. Aminophylline or a selective A1-adenosine receptor agonist can be used to detect viable myocardium and may be safer than dobutamine in severe chronic ischemic heart disease.

1087-98 Augmented Protein Expression of Neuronal Nitric Oxide Synthase in the Atria Parasympathetically Decreases Heart Rate During Acute Myocardial Infarction in Rats

Yoshihito Takimoto, Takeshi Aoyama, Reiko Keyamura, Yoshiki Yui, Shigetake Sasayama. *Kyoto University, Kyoto, Japan*

Background; Vagal stimulation has been reported to be associated with prevention of ventricular fibrillation after myocardial infarction (MI). Nitric oxide synthesized within sinoatrial cells and neurons has recently been shown to participate in cholinergic control of heart rate (HR). However, it is unknown whether nitric oxide in the neuronal cells in the heart plays a role in HR regulation after MI. **Methods;** One, 3, 7 and 14 days (n=6-10 for each group) after ligation of a coronary artery, we examined HR dynamics and neuronal nitric oxide synthetase (nNOS) expression in the atria by Western blotting. **Results;** The nNOS protein level in the atria was increased 4.5+0.5-*, 3.5+0.2-*, 1.7+0.1-* and 1.0+0.1-fold (*p<0.01) compared to that in sham-operated rats (SR) one, 3, 7 and 14 days after MI, respectively. Mean HR at baseline was 470+6 (p<0.01 vs. SR) and 378+4 in the MI group, and 398+13 and 375+4 in SR at 1 and 14 days post-infarct, respectively. To examine the role of nNOS on HR, a specific inhibitor of nNOS, 1-(2-trifluoromethylphenyl) imidazole (TRIM), was infused (50mg/kg i.v.). Increased HR after infusion of TRIM was 66+12*, 59+4*, 32+3* and 6+4 (*p<0.01 vs. SR) in MI rats, and 8+4, 6+3, 6+4 and 4+3 in SR one, 3, 7 and 14 days after MI, respectively. The effect of TRIM on HR was abolished by the prior administration of L-arginine (25mg/kg, i.v.). After the parasympathetic blockade with atropine (0.5mg/kg i.p.), the administration of TRIM did not significantly increase the HR in both rats with MI (7+5) and controls (0+4) one day post-infarct. Whereas, administration of TRIM with pretreatment of propranolol (1mg/kg i.v.) led to significant (p<0.01) heart rate increase in rats with MI (55+3) compared with that in sham-operated rats (14+3) one day post-infarct. There was a strong correlation (r=0.837, p<0.0001) between the nNOS protein expression and heart rate change after TRIM infusion. **Conclusion;** These results indicate that nNOS parasympathetically decreased heart rate via the production of nitric oxide in rats with acute MI. Thus, augmented expression of nNOS in the atria after acute MI reduces HR and may have beneficial effects on the heart by reducing O2 consumption and preventing ventricular fibrillation.

1087-99 Myoglobin Sustains Cardiac Function During Ischemia and Facilitates Oxygen Diffusion in the Beating Heart

Marc W. Merx, Ulrich Flögel, Axel Gödecke, Ulrich K. M. Decking, Jürgen Schrader. *Institut für Herz- und Kreislaufphysiologie, Heinrich Heine Universität, Düsseldorf, Germany*

Background: Myoglobin, an intracellular oxygen binding heme protein is considered a key player in intracellular oxygen supply with three main functions: facilitating oxygen diffusion, serving as oxygen reservoir and mediating oxidative phosphorylation. The recent generation of myoglobin knockout mice (myo-/-) in our laboratory led to a surprisingly benign phenotype, challenging myoglobin´s functional relevance. **Methods:** Here we explored the effect of acute carbon monoxide (CO) inhibition of myoglobin on isolated, Langendorff perfused hearts with hearts from myo-/- mice serving as appropriate controls. To closely mimic the in vivo situation, myoglobin oxygen saturation was measured in the beating heart utilizing 1H-NMR spectroscopy with arterial buffer-oxygen content being adjusted accordingly. **Results:** Acute myoglobin inhibition had no effect on oxidative phosphorylation. Partial deoxygenation (13%, determined by 1H-NMR) of myoglobin, being a prerequisite of facilitated diffusion, was achieved at an arterial buffer-oxygen content of 65%. Under these conditions we found that acute CO inhibition of myoglobin leads to decreased contractility (11% left ventricular developed pressure decrease in wt hearts vs. no change in myo-/- hearts, P<0.001) and increased coronary venous pO2 (plus 25% vs. no change, P<0.001), reflecting decreased myocardial oxygen consumption. When hearts were subjected to brief, no-flow ischemia both chronic and acute myoglobin inhibition resulted in a more pronounced functional decrease compared to wild type (wt) hearts (i.e. developed pressure decreased by 8.1±2.9% in myo-/- and CO treated wt hearts vs. 4.3±0.9% in control wt hearts, P<0,005). **Conclusion:** Carbon monoxide is a highly selective inhibitor of myoglobin. Oxidative phosphorylation is not mediated by myoglobin. During brief periods of ischemia myoglobin´s oxygen reservoir is responsible for sustainment of cardiac function. Myoglobin is important in facilitating the diffusion of oxygen from the vasculature to mitochondrial cytochromes in the beating heart.

1087-100 Administration of an Adenosine A2A Receptor Agonist (ATL-146e) Significantly Reduces Infarct Size in a Canine Model of Coronary Occlusion and Reperfusion

David K. Glover, Mirta Ruiz, Laurent M. Riou, Kazuya Takehana, Philip W. Smith, Jayson M. Rieger, Timothy L. Macdonald, Denny D. Watson, Joel Linden, George A. Beller. *University of Virginia, Charlottesville, VA*

Background: In recent clinical trials, adenosine has been shown to be cardioprotective by limiting infarct size when administered during reperfusion therapy, however the mechanism for this protection remains unknown. We sought to determine whether low dose administration of a highly potent and selective adenosine A_{2A} receptor agonist, ATL-146e, might also protect myocardium from infarction.

Methods: Accordingly, 7 open-chest dogs underwent 90 minutes of total left anterior descending (LAD) coronary occlusion with all visible collateral vessels tied, followed by 2 hours of reperfusion. Both core and heart surface temperatures were monitored and controlled to maintain a constant surface temperature (37°C). In a subset of these dogs (n=3), ATL-146e was infused i.v. at a concentration below that which produces vasodilatation (0.01 μg/kg/min) beginning immediately prior to the occlusion and continuing throughout reperfusion. Regional myocardial blood flow was measured using microspheres and myocardial risk area and infarct size were determined by blue dye and histochemical staining.

Results: During LAD occlusion, endocardial and transmural flows in the central infarct zone were similar in both the control (endo: 0.10 ± 0.01; tm: 0.12 ± 0.03 ml/min/g) and ATL-146e treated dogs (endo: 0.09 ± 0.02; tm: 0.15 ± 0.01 ml/min/g) (p=NS). After reperfusion, endocardial and transmural flows were also similar confirming that there was no vasodilatory effect of low dose ATL-146e. In addition, the myocardial area at risk was 31 ± 3% and 30 ± 5% of the left ventricle in the respective groups (p=NS). Despite a comparable level of flow reduction and similar risk areas, there was a significant 37% reduction in myocardial infarct size (% risk area) in the ATL-146e treated dogs (37 ± 6%) compared with the control dogs (59 ± 5%) (p<0.05).

Conclusion: The adenosine A_{2A} receptor agonist ATL-146e is cardioprotective in this canine model of infarction. This finding suggests that the mechanism for the adenosine-mediated protection observed in the clinical setting may involve the adenosine A_{2A} receptor pathway. The protective effect does not require the enhancement of blood flow.

1087-101 The Effect of Inotropic State on the Size of the Mitral Annulus

Joseph H. Gorman, III, Robert C. Gorman, Benjamin M. Jackson, Martin St.John-Sutton, Theodore Plappert, T. Sloane Guy, IV, Sina L. Moainie, L. Henry Edmunds, Jr.. *University of Pennsylvania School of Medicine, Philadelphia, PA*

Introduction: The mitral valve annulus is a dynamic structure whose function is intimately related to left ventricular (LV) performance. Chronic ischemic LV dysfunction can lead to annular dilatation which contributes to mitral regurgitation (MR). Using sonomicrometry array localization (SAL) imaging in sheep, we tested the hypothesis that changes in LV inotropic state directly affect the size of the mitral valve annulus. SAL accurately determines the three-dimensional spatial relationships of sonomicrometry transducers every 5 ms throughout the cardiac cycle. **Methods:** In 6 sheep, 6 transducers were sutured around the mitral annulus. One week after instrumentation, animals were b-blocked with esmolol (mean infusion 6.7 ± 3.5 mg/min) to a rate of 90 bpm and were atrially paced; SAL was recorded at heart rates of 120 bpm and 150 bpm. Esmolol was discontinued and the animals allowed to return to steady state. An isoproterenol infusion was titrated to produce rates of 120 bpm (mean infusion 4.6 ± 3.9 mg/min) and 150 bpm (mean infusion 5.5 ± 4.1 mg/min), and SAL data recorded at both heart rates. Thermodilution cardiac outputs (CO) were acquired in triplicate at all physiologic conditions. All statistical comparisons were made between isoproterenol and atrially-paced groups at the same heart rate using paired t-test, and the values reported as mean ± standard deviation. **Results:** At a rate of 120 bpm, the atrially-paced group had CO of 2.8 ± 0.5 L/min and end systolic (ES) annular area of 780 ± 150 mm2. At the same rate, the isoproterenol group had significantly increased (p<0.004) CO of 4.5 ± 1.0 L/min and significantly decreased (p<0.002) ES annular area of 700 ± 160 mm2. At a rate of 150 bpm, the atrially-paced group had CO of 3.2 ± 0.5 L/min and end systolic (ES) annular area of 750 ± 130 mm2. At the same rate, the isoproterenol group had significantly increased (p<0.004) CO of 5.8 ± 1.5 L/min and significantly decreased (p<0.002) ES annular area of 650 ± 150 mm2. **Conclusions:** Isoproterenol increases LV inotropic state and decreases mitral valve area independent of heart rate. These findings may have implications for the treatment of MR due to annular dilatation secondary to ventricular dysfunction.

1087-102 Na+/Ca2+ Exchange May Play an Important Role in Ischemia-Reperfusion Injury in In Vivo Heart and Brain

Teisuke Takahashi, Kenzo Takahashi, Michihito Onishi, Yu Tanaka, Tomomi Ota, Kazuya Kameo. *Taisho Pharmaceutical, Co., Ltd., Omiya, Japan*

Background: Activation of the reverse mode of Na+/Ca2+ exchange may contribute to Ca2+ overload during reperfusion after transient ischemia. Role of Na+/Ca2+ exchange in in vivo myocardial and cerebral ischemia-reperfusion injury was examined by using SEA0400, a novel potent and selective Na+/Ca2+ exchange inhibitor. **Methods and Results:** In the rat ischemia-reperfusion arrthymia model, ischemia was induced by 5-min occlusion of the left anterior descending coronary artery followed by 10-min reperfusion. SEA0400, administered 1 min before reperfusion, at 1 mg/kg i.v. reduced the incidence of ventricular fibrillation from 80 to 20% (P < 0.05) and mortality from 70 to 20% (P < 0.05). In the dog coronary occlusion model, myocardial stunning was caused by 15-min occlusion of the left anterior descending coronary artery followed by 4-hr reperfusion. SEA0400, administered 1 min before reperfusion, at 1.0 mg/kg i.v. improved recovery of myocardial segment shortening of the ischemic region after 4-hr reperfusion period: 77±8% compared with vehicle (45±8%) (P < 0.05). In the rat focal cerebral ischemia-reperfusion model, ischemia was induced by the 2-hr occlusion of the middle cerebral artery followed by 24-hr reperfusion. SEA0400, administered after occlusion, at 3 mg/kg i.v. bolus + 3 mg/kg/hr i.v. infusion reduced infarction volume: 109±25 mm3 compared with vehicle (197±23 mm3)(P < 0.05). **Conclusion:** These results suggest that activation of Na+/Ca2+ exchange play an important role in ischemia-reperfusion injury in in vivo heart and brain. Thus, inhibition of Na+/Ca2+ exchange may provide a novel therapeutic strategy to reduce myocardial and cerebral reperfusion injury.

ORAL CONTRIBUTIONS

801 Featured Oral Abstract Session: Insights Into Myocardial Remodeling

Monday, March 19, 2001, 9:15 a.m.-10:30 a.m.
Orange County Convention Center, Valencia A

9:30 a.m.

801-2 The Effect of Early Post-infarction Mitral Regurgitation on Late Ventricular Remodeling

Robert C. Gorman, Joseph H. Gorman, III, Benjamin M. Jackson, T. Sloane Guy, IV, Sina L. Moainie, Theodore Plappert, Martin St.John-Sutton, L. Henry Edmunds, Jr.. *University of Pennsylvania School Of Medicine, Philadelphia, Pa*

Background: The Question Of How Post-infarction Mitral Regurgitation (Mr) Affects Left Ventricular (Lv) Function Over Time Is Incompletely Understood. We Studied Two Types Of Posterolateral Infarctions In Sheep, One Which Produces Mr And One Which Does Not, To Examine The Contribution Of Ischemic Mr To Lv Remodeling And Congestive Heart Failure (Chf). **Methods:** Group A (n=5) had infarction of 25% of the LV mass localized to the posterolateral ventricle, resulting in a compensated infarction which does not lead to CHF. Group B (n=5) had infarction of 25% of the LV mass localized to the posterolateral ventricle and including the posterior papillary muscle, resulting in acute development of MR and leading to severe CHF. Transdiaphragmatic echocardiograms were used to measure end-systolic (ES) LV sphericity (the ratio of minor axis to major axis diameter) and ES LV volume, as well as to assess the degree of MR. **Results:** In group A, no animal developed MR, ES LV volumes increased by 71% over 8 weeks, and LV sphericity increased from 0.45 at baseline to 0.50 (NS) at 8 weeks. In group B, the mean degree of MR immediately postinfarction was 2.7. The MR progressed to a mean of 3.2 at 8 weeks. In this group, ES LV volumes increased by 140% over 8 weeks, and LV sphericity increased from 0.43 at baseline to 0.56 ($p < .05$) at 8 weeks. At 8 weeks, the two groups had significantly different LV volumes and sphericities ($p < .05$). **Conclusions:** These results indicate that significant early post-infarction MR is progressive and greatly exacerbates post-infarction LV remodeling. This data suggest that surgical intervention to treat early post-infarction MR may convert an uncompensated infarct destined to result in CHF to a compensated infarct consistent with adequate long-term hemodynamic function.

9:45 a.m.

801-3 Macrophage-Colony Stimulating Factor (M-CSF) Induction in the Infarcted Myocardium Is Associated With Macrophage Differentiation and Proliferation and May Promote Tissue Remodeling

Nikolaos G. Frangogiannis, Leonardo H. Mendoza, Oliver Dewald, Lloyd H. Michael, C Wayne Smith, Mark L. Entman. *Baylor College of Medicine, Houston, TX*

Background: Myocardial infarction is associated with a rapid induction of mononuclear cell chemoattractants, such as Transforming Growth Factor-β and Monocyte Chemotactic Protein-1, leading to monocyte infiltration in the injured area. Effective healing is dependent on survival and differentiation of infiltrating monocytes to macrophages. We hypothesized that the monocyte to macrophage differentiation factor M-CSF may be induced in the infarcted myocardium and may modulate monocyte phenotype. **Methods:** We used a canine model of myocardial infarction and an in vitro model of isolated canine mononuclear cells. **Results:** Using RT-PCR we obtained a cDNA clone for canine M-CSF. We demonstrated marked induction of M-CSF mRNA in ischemic segments starting after 3 h of reperfusion and peaking after 24 h of reperfusion. M-CSF was predominantly localized in macrophages infiltrating the injured myocardium. We used staining with the myeloid cell marker Mac-387 to identify newly recruited monocytes and with the anti-macrophage antibody PM-2K to label mature differentiated macrophages. Abundant Mac-387 positive cells were noted in the ischemic myocardium after 24 h of reperfusion (Ischemic: 495.6+148.6 cells/sq mm Versus control: 6+1.95; $p<0.01$, $n=4$) indicating active recruitment of new myeloid cells. In contrast, after 7 days of reperfusion the number of newly recruited Mac-387 expressing cells decreased (74.05+8.67, $n=4$) and the majority of inflammatory cells in the healing scar were PM-2K positive, Mac387 negative macrophages. Dual immunostaining demonstrated significant numbers of proliferating PCNA positive macrophages in the scar. Macrophage accumulation was associated with marked upregulation of Osteopontin(OPN)-1, a marker of monocyte to macrophage differentiation. *In vitro* experiments showed that M-CSF induced expression of OPN and matrix metalloproteinase (MMP)-9 in isolated canine mononuclear cells. **Conclusion:** We suggest that the local upregulation of M-CSF in myocardial infarcts may promote macrophage differentiation and proliferation, and modulate monocyte phenotype, allowing them to play an active role in tissue remodeling through the expression of MMPs.

10:00 a.m.

801-4 Effects of Angiotensin II Receptor Blockade, Angiotensin-converting Enzyme Inhibition, and Their Combination on Postinfarction Ventricular Remodeling

Sunil Mankad, Nathaniel Reichek, Deepak Singh, Walter J. Rogers, Christopher M. Kramer. *Allegheny General Hospital, Pittsburgh, PA, University of Virginia Health System, Charlottesville, VA*

Angiotensin-converting enzyme inhibition (ACEI) attenuates post-infarction LV remodeling, but effects of angiotensin II type 1 receptor antagonism (AT_1A) alone or in combination with ACEI are unclear. Accordingly, we studied the effects of AT_1A, standard dose ACEI (sACEI), high dose ACEI (hACEI), and combined AT_1A + sACEI on post-infarction LV remodeling in a well-characterized ovine model. **Methods:** Two days after transmural anteroapical myocardial infarction by coronary ligation, 62 sheep were treated with either no therapy (Control, n=12), sACEI (ramipril 10 mg/day, n=14), hACEI (ramipril 20 mg/day, n=8), AT_1A (losartan 50 mg/day, n=13), or combination therapy with AT_1A + sACEI (CT; ramipril 10 mg/day + losartan 50 mg/day, n=15). Magnetic resonance imaging (MRI) was performed before and 8 weeks after myocardial infarction to quantify changes in LV end-diastolic volume index (EDVi), end-systolic volume index (ESVi), and ejection fraction (EF). Regional % intramyocardial circumferential shortening (%S) in noninfarcted segments adjacent to the infarct (within 2 cm) was measured using tagged MRI. **Results:** Infarct size, mean systolic blood pressure, and left atrial pressure at 8 weeks post-infarction were similar between groups. Heart rate at 8 weeks post-infarction was significantly higher in the Control group compared to sACEI, hACEI, AT_1A, or CT groups, respectively: 124±17*, 102±12, 104±15, 111±12, and 107±12; $p<0.001$). Baseline EDVi, ESVi, EF, and adjacent %S were similar. CT resulted in the most marked blunting of LV remodeling (change from baseline):

	ΔEDVi ml/kg)	ΔESVi (ml/kg)	ΔEF (%)	ΔAdjacent %S (%)
Control	+0.9±0.1	+1.0±0.1	-23±2	-8±1
sACEI	+0.7±0.1	+0.7±0.1	-18±2	-7±1
hACEI	+0.6±0.2	+0.6±0.1Ý	-14±3Ý	-5±1
AT_1A	+0.9±0.1	+0.9±0.1	-18±3	-5±1
CT	+0.4±0.1#	+0.4±0.1*	-11±2*	-2±1*

(*p<0.04 vs sACEI, AT_1A and Control; p<0.05 vs Control; #p <0.003 vs AT_1A and Control; ANOVA; mean±SE). **Conclusion:** Compared to sACEI, hACEI, or AT_1A, combined sACEI + AT_1A is superior at attenuating LV remodeling and limiting systolic dysfunction following myocardial infarction.

10:15 a.m.

801-5 ACE Inhibition, AT1- and ETA-Receptor Antagonism: Comparison of Structural Reorganization of the Myocardium After Infarct in Stroke Prone Spontaneously Hypertensive Rats

Alexander Reinecke, Quingui Xia, Marc Dorenkamp, Susanne Penz, Christian Stotz, Harro Bitterling, Rüdiger W.R. Simon and Thomas Unger. *Clinic of Cardiology, University of Kiel, Kiel, Germany, Institute of Pharmacology, University of Kiel, Kiel, Germany*

Background: The structural organization of the myocardial collagen network plays a major role in post infarct remodelling and left ventricular (LV) dilation. **Methods:** We investigated the ability of the ETA receptor antagonist, Lu 135252 (Lu) (30 mg/kg/d), to reduce fibrosis in the infarcted and noninfarcted myocardium and LV dilation in stroke-prone spontaneously hypertensive rats. Six weeks after induction of myocardial infarction (MI), the effects of Lu were compared with those of the AT1 receptor antagonist, irbesartan (Irb) (50 mg/kg/d), the ACE inhibitor, fosinopril (Fos) (20 mg/kd/d) and placebo treated controls. Treatment was started 4 weeks prior to induction of MI and continued up to 6 weeks post MI. Picrosirius red stained myocardial sections were examined using circularly polarized light and a digitized morphometric system. **Results:** Lu reduced both, the total collagen content (3.19 + 0.09 (Lu) vs 3.99 + 0.06 (Irb), 4.72 + 0.16 (Fos),and vs 6.85 + 0.13 (controls) (% of volume fraction)) and the proportion of thick collagen fibers (64.14 + 5.22 (Lu) vs 84.66 + 4.44 (Irb), 76.37 + 6.1 (Fos) and 90.01 + 7.43 (controls) (% of total collagen content)) to a significantly ($p<0.01$ - $p<0.001$) greater extent than Irb or Fos. Compared to all other groups, treatment with Lu also markedly increased LV circumference and diameter ($P<0.05$) after MI. **Conclusion:** The association of LV dilation with a) reduction of total collagen content and b) lower proportion of thick collagen fibers after chronic treatment with Lu suggests that balanced myocardial fibrosis is a prerequisite to maintain structural integrity after myocardial infarction. Thus, the adaptive reorganization of appropriate collagen fibers after MI was better achieved by treatment with Irb and Fos than with Lu.

ORAL CONTRIBUTIONS

820 Acute Coronary Syndromes: Cardiac Markers in Risk Assessment and Management Decisions

Monday, March 19, 2001, 11:00 a.m.-12:15 p.m.
Orange County Convention Center, Room 230B

11:00 a.m.

820-1 Troponin T and I to Predict 6 Month Mortality and Relative Benefit of Invasive vs. Conservative Strategy in Patients With Unstable Angina: Primary Results of the TACTICS-TIMI 18 Troponin Substudy

Christopher P. Cannon, William S. Weintraub, Laura Demopoulos, Ralph Vicari, Martin J. Frey, Nasser Lakkis, Debbie Robertson, Paul deLucca, Nader Rifai, Eugene Braunwald, for the TACTICS-TIMI 18 Investigators. *Brigham and Women's Hospital, Boston, MA*

Measurement of troponin (Tn) T and I have been useful in assessing prognosis in patients with unstable angina. In addition, greater benefit from glycoprotein IIb/IIIa inhibitors is achieved in patients with elevated troponin values than in patients without elevated Tn values. Their use in predicting benefit of an invasive vs. conservative strategy has not

yet been established. **Methods:** In the TACTICS-TIMI 18 trial patients with unstable angina or non-ST elevation MI were treated with aspirin, heparin and tirofiban and randomized to an invasive strategy with routine catheterization and revascularization as appropriate within 4-48 hours, or to a conservative (i.e., a "selective invasive" strategy) with catheterization performed only if the patient had objective evidence of recurrent ischemia or a positive stress test. Both troponin T and I were measured in all patients who provided a baseline blood sample (N=1763). **Results:** Preliminary results as of August 2000 showed a graded increase in the 6-month mortality rate for both troponin values.(See table)

TnT	<=0.01	>0.01-0.06	>0.06-9.1	>0.1-1.0	>1.0	P Trend
N=	808	150	81	527	197	
Mortality (%)	1.9	3.3	2.5	3.8	5.1	0.009
TnI	<0.1	>0.1-0.4	>0.4-1.0	>1.0-1.5	>1.5	P Trend
N=	394	79	70	37	1183	
Mortality (%)	1.3	0	5.7	13.5	3.3	0.034

Conclusion: Both TnT and I were significant predictors of 6 month mortality. Their use in predicting benefit of a routine invasive vs. "selective invasive" strategies will be presented.

11:15 a.m.

820-2 **Troponin-T 0.03 ug/L Is the Most Appropriate Cut-Off Level Between High and Low Risk Acute Coronary Syndrome Patients: Prospective Verification in a Large Cohort of Placebo Patients From the GUSTO-IV ACS Study**

B Lindahl, P Venge, P Armstrong, E Barnathan, R Califf, M Simoons, E Topol, Lars Wallentin. *Department of Cardiology, Uppsala, Sweden*

The prognostic value of troponin T (tnT) in unstable coronary artery disease (UCAD) is well established. A 3rd generation tnT assay using human recombinant cardiac tnT for calibration has been developed improving precision and modifying the measuring range. The upper reference level of healthy controls with this new assay is below the detection limit 0.01 ug/L. Considering the precision of the assay a new cut-off value of 0.03 ug/L was recently recommended based on retrospective analysis in relation to outcome in 2156 noninvasively managed patients in the FRISCII trial. In order to prospectively verify this new cut-off we tested its relation to the 30 days rate of death or MI in a large cohort of placebo patients in the GUSTO-IV-ACS trial. **Methods:** Plasma sample obtained at inclusion in 2160 of the 2598 enrolled in the placebo group of the GUSTOIV ACS trial recruiting patients within 24 hours after the last episode of chest pain and with ST-segment derpession or elevation of a biochemical marker of myocardial damage. All placebo patients were treated with aspirin and heparin or lmw heparin. The primary end-point was death or MI at 30 days. Serum samples were obtained at entry and analysed in the core laboratory with the 3rd generation tnT assay (Roche Diagn.) with a detection limit of 0.01 ug/L and a functional sensitivity (CV<20%) of 0.03 ug/L.

Results concerning death or MI% at 30 days

Troponin-T ug/L	<0.03	0.03-<0.1	0.1-<0.3	>=0.3
Patients	818	276	388	678
Death	1.6%	2.5%	4.6%	6.8%
Death or MI	4.0%	9.1%	9.5%	9.7%

Conclusion: The results confirm that a cut-off level Troponin-T 0.03 ug/L is the most appropriate for identification of patients with minor myocardial infarction and a raised risk for subsequent events.

11:30 a.m.

820-3 **Are There High-Risk Patients Who Are Troponin Negative? Further Risk Stratification With the TIMI Risk Score in Patients With Acute Coronary Syndromes: Results From OPUS-TIMI 16**

Christopher P. Cannon, Carolyn H. McCabe, Elliott M. Antman, Jane Bentley, Nader Rifai, Eugene Braunwald. *Brigham and Women's Hospital, Boston, MA*

While patients who are troponin (TnI) positive are at high risk of mortality and recurrent cardiac events, debate has emerged about patients who are troponin negative. Are they all low-risk? We hypothesized that clinical risk factors can identify patients at high risk of mortality even among patients who are troponin negative. **Methods:** In the OPUS-TIMI 16 trial, patients with acute coronary syndromes (ACS) were treated with aspirin and randomized within 72 hours of symptom onset to the oral IIb/IIIa inhibitor orbofiban or placebo. In a case-control study of the composite endpoint of death, MI, urgent revascularization, recurrent ischemia requiring rehospitalization or stroke, TnI (Bayer) was measured in 2241 patients at study entry, and the TIMI Risk Score was calculated for each patient using 6 of the 7 criteria. **Results:** Patients with TnI > 0.1 ng/ml had increased relative risk (RR) of 10 month mortality RR=1.6, p=0.03, MI RR=1.82, p=0.001, death or MI, 10 months RR=1.7, p=0.0002, urgent revascularization RR=1.56, p=0.004, and death/MI/urgent revascularization RR=1.82, p<0.0001, but only weakly for the composite including angina requiring rehospitalization: RR=1.17, p=0.043. Among patients with a negative troponin <= 0.1 ng/ml, the TIMI Risk Score identified a graded increase in the relative risk of the composite endpoint to 10 month follow-up (TRS 0, RR=1, TRS 1,2,3,4, 5-6 Rel Risk: 1.3, 1.4, 1.8, 2.3, 2.6, p trend = 0.002. **Conclusion:** In this broad population of patients with acute coronary syndromes, TnI was a significant predictor of long-term mortality and ischemic events. Most importantly, however, among patients with a negative troponin, formerly considered to be low-risk patients, the TIMI Risk Score was able further risk stratify patients into high and low risk. These data indicate that additional risk stratification should be carried out beyond just assessment of troponin in order to identify high-risk patients who warrant aggressive therapy.

11:45 a.m.

820-4 **No Beneficial Effect of 24-48 Hours Abciximab Infusion in Aspirin and Heparin Treated Acute Coronary Syndrome Patients With Elevated Troponin Without Early Revascularisation Procedures: a GUSTO-IV ACS Substudy**

S James, B Lindahl, P Venge, P Armstrong, E Barnathan, R Califf, M Simoons, E Topol, L Wallentin. *Dept of Cardiology, Uppsala, Sweden*

In acute coronary syndrome (ACS) elevation of troponin (Tn) level is associated with a raised risk of subsequent cardiac events. In the GUSTOIV ACS trial outcome in relation to Tn was a predefined substudy. **Methods:** The multinational multicenter prospective double-blind trial of the efficacy of abciximab as the primary medical treatment in ACS without early revascularization included 7800 patients with chest pain within 24 hours and either ST-segment depression or elevation of troponin at entry. The patients were randomized to bolus injection followed by 24 hours (n=2590) or 48 hour (n=2612) infusion of abciximab or corresponding placebo (n=2598). TnT was measured by the 3rd generation Elecsys method at the core laboratory in samples obtained at randomization from 6525 patients. Elevated Tn was also reported in the CRF according to local methods at each centre. Primary endpoint was death or MI at 30 days by intention-to-treat which was related to the predefined cut-off level of 0.1 ug/L for the core laboratory Tn

Results concerning death or MI% at 30 days

Local Tn	Placebo	Abc24	Abc24	Placebo	Abc24	Abc48
Negative	n=978	n=925	5.4%	6.8%	7.5%	
Positive	n=1329	n=1361	n=1351	10.0%	9.1%	9.3%
TnT	Placebo	Abc24	Abc24	Placebo	Abc24	Abc48
<0.1 ug/L	n=1094	n=1082	n=1090	5.3%	5.9%	6.0%
>=0.1 ug/L	n=1066	n=1099	n=1094	9.7%	10.2%	11.7%

Conclusion: In accordance with previous reports elevated troponin levels identify patients with higher risks of subsequent death or MI. However, the present prospective study does not confirm the concept that elevated troponin levels will identify responders to treatment with GpIIb/IIIa inhibitors.

Noon

820-5 **Risk Stratification in Unstable Angina: Incremental Analysis of Clinical, Electrocardiographic, Autonomic and Biochemical Markers**

Simon R. O. Kennon, Heather Clarke, James Hooper, Jackie Cooper, Adam D. Timmis. *Barts and the London NHS Trust, London, United Kingdom*

Background: The positive predictive values of tests used for risk stratification in non-ST-elevation acute coronary syndromes are generally low. Incremental analysis has the potential to enhance predictive value but there have been few reports of its application in this group of patients. In this study the incremental value of clinical data, troponin T, ST segment monitoring and heart rate variability for predicting outcome in patients with non-ST-elevation acute coronary syndromes has been evaluated.
Methods: Prospective cohort study of 304 consecutive patients admitted with non-ST-elevation acute coronary syndromes. Baseline clinical and electrocardiographic data were recorded, serial blood samples obtained for troponin T assay, and 48 hour Holter monitoring performed for ST segment and heart rate variability analysis. End-points were major ischaemic events (cardiac death, non-fatal myocardial infarction) during follow-up for 12 months.
Results: After 12 months, 7 patients had died and 21 had had non-fatal myocardial infarction. The risk of an event was increased by troponin T >0.1µg/l (odds ratio 6.33; 95% confidence intervals 1.9-21.09), T wave inversion on the presenting ECG (5.75; 1.48-22.25), Holter ST elevation (4.41; 1.51-12.92), Holter STdepression (3.24; 1.11-9.43), and a decrease in the standard deviation of 5 minute mean RR intervals (0.53; 0.29-0.96). Positive predictive values of individual multivariate risk markers for cardiac death and non-fatal infarction in the first year were low, however, incremental analysis of all multivariate risk markers permitted calculation of a cumulative risk score which increased the positive predictive value to 46.9% while retaining a negative predictive value of 96.9%.
Conclusion: An incremental approach to risk stratification in non-ST-elevation coronary syndromes, utilising a range of widely available risk markers, was powerfully predictive of outcome, successfully identifying a group in whom the risk of cardiac death or non-fatal myocardial infarction approached 50% during the first 12 months.

ORAL CONTRIBUTIONS

821 Stabile Ischemic Syndrome: Clinical Aspects

Monday, March 19, 2001, 11:00 a.m.-12:15 p.m.
Orange County Convention Center, Valencia A

11:00 a.m.

821-1 Improvement in Health Status at 3 Months in the COURAGE Trial: Seattle Angina Questionnaire Results

William S. Weintraub, John Spertus, Emir Veledar, Cheryl Lewis, Elizabeth Mahoney, Pamela Hartigan, David J. Maron, Koon Teo, Paul Casperson, Karen Potter, Sandra B. Dunbar, Robert A. O'Rourke, William E. Boden. *Emory University, Atlanta, GA, West Haven Veterans Administration Hospital, West Haven, CT*

Background: The utility of percutaneous coronary intervention (PCI) to treat angina is being evaluated in COURAGE, a multicenter randomized trial in 3260 patients treated with best possible medical care and randomized to medicine vs medicine plus PCI.
Methods: COURAGE includes a detailed health related quality of life (QOL) study, with angina measured using the Seattle Angina Questionnaire (SAQ). COURAGE also includes aggressive treatment goals for angina (angina free), blood pressure, exercise, diabetes control and lipid lowering, all according to ACC/AHA guidelines. The SAQ includes domains for physical limitation, angina stability, angina frequency, treatment satisfaction and QOL. Scores can range from 0 to 100, with higher scores reflecting better status.
Results: Baseline and three month SAQ scores are available for the first 195 patients randomized in COURAGE:

	Baseline	3 Months	P Value
Physical Limitation	63±27	72±26	0.0008
Angina Stability	48±33	76±28	<0.0001
Angina Frequency	64±28	80±24	<0.0001
Treatment Satisfaction	86±18	91±12	0.0012
Quality of Life	47±26	68±26	<0.0001

The physical limitation, anginal stability, anginal frequency and QOL scales all improved significantly. SAQ scores were correlated with treatment goal variables. Physical limitation at 3 months correlated with targets for no angina (p=0.081), regular exercise (p=0.0038) and LDL <85 mg/dl (p=0.075). Angina stability correlated with target for no angina (p=0.0004). Angina frequency correlated with target for no angina (p=0.0001), systolic pressure <130 (p=0.048) and diastolic pressure <80 (p=0.025). QOL correlated with target for no angina (p=0.0001).
Conclusions: Patients with coronary disease and significant angina can be expected to improve over a period of several months with aggressive treatment options including PCI and medical management. The Seattle Angina Questionnaire offers a detailed assessment of anginal burden on health related QOL and correlates with other measures of outcome. The importance of intensive medical therapy as an adjunct to PCI in symptomatic CHD patients can be demonstrated to improve health outcomes using the SAQ in a large randomized trial.

11:15 a.m.

821-2 Percutaneous Myocardial Laser Revascularisation (PMR): Is the Symptomatic Benefit Maintained to 2 Years?

Richard J. Allen, Simon R. Redwood, D J. Coltart. *Guy's and St Thomas' Hospital Trust, London, United Kingdom*

Between May '98 and September '99, patients with Canadian Cardiovascular Society (CCS) class III or IV angina were entered into a longitudinal study into the effects of PMR. All patients were unsuitable for more conventional methods of revascularisation. **Method.** PMR was performed on 27 patients (22 male) using the CardioGenesis PMR system. At follow up patients were assessed for CCS angina class, exercise treadmill testing (Naughton protocol) and completed the Seattle Angina Questionnaire to assess impact on quality of life. Nuclear myocardial perfusion scanning was performed at baseline and 6 months follow up. **Results.** Angina class improved from 3.45 ± 0.3 (mean ± SD) to 2.09 ± 0.6 at 3 months (p<0.001). There was at a 2+class improvement in 67% of patients at 3 months. The improvements were maintained to 6 months (p<0.001), but thereafter a gradual return of symptoms was reported. At 1 year there was still a significant improvement in angina (p<0.05) but at 2 years angina levels (3.16 ± 0.4) have virtually returned to baseline (p=NS). Exercise capacity increased from 342 ± 202 seconds to 470 ± 252 seconds at 3 months (p<0.001). The improvements were maintained to 1 year, 432 ± 232 seconds (P<0.01) but were again reduced at 2 years (p = NS). Quality of life measures were significantly improved at 3 months (p<0.01) with the benefits maintained to 2 years (p<0.01). No significant improvements were detected on nuclear perfusion scanning at 6 months (p=NS). **Conclusions.** PMR offers hope to a group of patients who have little in the way of therapeutic options. Our findings suggest significant initial symptomatic benefits lasting to 6 months, after which there is a gradual return in symptoms, with no significant anginal improvement 2 years after the procedure. The findings are interesting with regards to the potential mechanism of action of PMR and call into question how worthwhile the treatment is long-term.

11:30 a.m.

821-3 Protective Effects of Angiotensin Converting Enzyme Inhibitors in African American Men With Coronary Artery Disease

Vasilios Papademetriou, Andreas Pittaras, Peter Kokkinos, Puneet Narayan. *VA Medical Center, Washington DC, DC, Georgetown University, Washington, DC*

Background: Angiotensin converting enzyme inhibitors (ACEI) are underutilized in African-Americans (AA) because of their perceived lesser efficacy in the control of hypertension. However, the potential protective effect of ACEI in AA has not been evaluated.
Methods: We assessed the effects of ACEI therapy in 810 AA men who underwent diagnostic cardiac catheterization at the Washington VAMC.
Results: Of those, 237 (29%) received ACEI therapy and 573 (71%) did not. All patients received adjunctive therapy (BB, CCB, diuretics, and cholesterol lowering agents) as needed. Both groups were of similar age at entry (68±10 Vs 68±9 yr.) had similar lipid profiles and blood pressure. Patients on ACEI however were heavier (84±16 Vs 81±14 kg; p <0.02), had higher blood glucose (132±37 Vs 123±32 mg/dl; p<0.001, had higher LVMI (166±49 Vs 156±49; p<0.01) and lower EF (49% Vs 58%; p<0.000). More patients in the ACEI group had diabetes mellitus (43% Vs 27.5%; p<0.000), severe CAD (36% Vs 28%; p<0.03), history of hypertension (75% Vs 64%; p<0.004), complex arrhythmias (21.8% Vs 14.4%; p<0.01), and CHF (26.7% Vs 9.5%; p<0.000). Over a period of 120±28 months, 74 patients (31%) in the ACEI group and 212 (37%) in the non-ACEI group died. After adjusting for confounding factors (Cox Regression), patients not receiving ACEI had 80% higher mortality compared to patients on ACEI (RR=1.8; CI: 1.3-2.6; p<0.000).
Conclusion: These data indicate a strong protective effect of ACEI in AA men with coronary heart disease.

11:45 a.m.

821-4 What Strategy in Totally Asymptomatic Diabetic Patients With Myocardial Perfusion Defect at Stress SPECT Imaging Performed as a Screening Test?

Alexis Cerisier, Valérie Bruiport-Cerisier, Bruno Estour, Antoine Da Costa, Karl Isaaz. *University of Saint Etienne, Saint Etienne, France*

How to manage totally asymptomatic diabetic (TAD) patients in whom a myocardial perfusion defect has been documented by stress SPECT imaging performed as a screening test remains debated. A follow-up (F-U) registry recruited, from 03/92 to 03/97, 383 TAD pts (age 61 ±10 years, 192 males) without history of heart disease who underwent a rest Thallium 210/stress Tc-99m sestamibi SPECT imaging screening because of a diabetes duration > 10 years plus at least one additional risk factor. Among the 383 pts, 124 had at least one myocardial perfusion defect at SPECT and were managed at physician discretion either with conservative medical treatment (G1 n=60) or invasively with immediate coronary catheterization followed by revascularization whenever possible (G2 n=64). The mean F-U was 39 months (range 21-57). **Results.** At inclusion in the registry, the 2 groups did not differ regarding age, gender, duration of diabetes, number of risk factors; the extent of SPECT defects was greater in G2 (1.65) than in G1 (1.4, p = 0.04). The pharmacologic treatment during F-U was similar between the 2 groups. During F-U in G1, 15 pts (25 %) underwent coronary angiogram and 6 were revascularized (10 %); in G2, 2 pts underwent repeat coronary angiogram leading to revascularization in one. At F-U, cardiac death and combined major cardiac events (cardiac death, heart failure, acute myocardial infarction, unstable angina) rates were higher in G1 than in G2, relative risk (RR) 0,31(p=0.07; 95% CI 0,084 to 1,13) and RR 0,37 (p=0.0085; 95% CI 0,18 to 0,78), respectively. By univariate analysis, age, gender, diabetes duration, number of risk factors and extent of SPECT defect were not prognosis predictors whereas the non-invasive/invasive approach was. Thus, immediate invasive strategy may improve the prognosis of selected totally asymptomatic diabetic patients in whom myocardial perfusion defect has been documented by SPECT imaging performed as a screening test.

Noon

821-5 Are Women at Increased Risk of Death After PCI? Results From the ACC-NCDR Database

Vernon Anderson, William S. Weintraub, Richard Shaw, Charles McKay, Ralph Brindis. *On Behalf of the ACC-NCDR(TM)/ACC Database Committee, Bethesda, MD*

Background: Women are at increased risk after percutaneous coronary intervention (PCI). However, there are little data to quantify this increased risk from contemporary, nationally based, multisite registries. The ACC-NCDR is a major registry activity of the American College of Cardiology which is designed to assess outcome of PCI.
Methods: Outcome of PCI in men (n=11508) and women (n=5800) was examined in the ACC-NCDR database. 45 institutions (1/1/98-6/30/99) with acceptable complete data used standardized definitions and identical reporting standards.
Results: Women were older, more symptomatic, had more co-morbidity, but less objective severity of disease (see table).

	Men	Women	P Value
Age	62±12	66±12	<0.0001
Hypertension	59%	70%	<0.0001
Diabetes	23%	30%	<0.0001
Heart Failure	9.6%	14.4%	<0.0001
Class III-IV Angina	60%	64%	<0.0001
Prior CABG	21%	15%	<0.0001
Ejection Fraction	51±14	54±15	<0.0001
Stent	70%	68%	0.003
Angiographic Success	92%	93%	0.23

Q Wave MI	0.45%	0.47%	0.99
CABG	2.14%	2.51%	0.14
Death, All Cases	1.38%	2.23%	0.0001
Death, Elective Cases Only	0.46%	0.86%	0.01
Stay (days)	2.3±3.1	2.8±3.8	<0.0001

While no difference in non-fatal events was noted, women had higher mortality. However, corrected for baseline differences, there was only a trend toward increased mortality in women (OR = 1.27, 95% CI 0.97-1.65).

Conclusion: In the ACC-NCDR, women had higher in-hospital mortality than men, but primarily due to older age and greater co-morbidity. The broadly representative nature of the ACC-NCDR offers a nationally based registry to examine in-hospital outcome of PCI in the United States.

POSTER SESSION

1117 Stabile Ischemic Syndrome: New Mechanical Therapies

Monday, March 19, 2001, Noon-2:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 1:00 p.m.-2:00 p.m.

1117-75 Are the Initial Benefits of Enhanced External Counterpulsation Sustained at One Year?

William E. Lawson, John C. K. Hui, Elizabeth D. Kennard, Richard Holubkov, Sheryl F. Kelsey. *SUNY Stony Brook, Stony Brook, NY, University of Pittsburgh, Pittsburgh, PA*

Background: Enhanced external counterpulsation (EECP) has been shown to be a safe and effective treatment of angina in several small University hospital case series, with clinical benefits lasting up to five years in follow-up. However, there is no data on the long term effectiveness of EECP in routine clinical practice.

Methods: The International EECP Patient Registry (IEPR) was initiated in January 1998 at the University of Pittsburgh to sequentially track angina patients (pts) treated with EECP for up to 3 years across a broad spectrum of providers and practice settings. The registry records: pt demographics, Canadian Cardiovascular Society (CCS) Angina class, adverse cardiovascular events (MACE-including: hospitalization, death, infarction (MI), revascularization (PCI and CABG)). The IEPR first year follow-up is analyzed.

Results: The IEPR includes 734 angina pts one year post EECP, with completed follow-up available on 589 pts. Patients were predominately male (75%) with a mean age of 68 years. Pre treatment history was significant for: multivessel disease- 77.6%, prior angioplasty - 58.3%, prior CABG - 56.5%, prior MI - 63.5%, history of Congestive Heart Failure - 26.1%. The pts received a mean 34 hours of treatment with 83% completing the full course of treatment. Events occuring during the treatment period included: unstable angina in 2.5%, MI in 0.4%, death 0.1%, CABG 0.5%, PTCA in 0.1%. CCS Angina class immediately post EECP improved in 73.4% of pts and 61.6% of pts discontinued nitroglycerin use. The improvement in angina was maintained at 6 and 12 months (table). Cumulative MACE at 12 months included: death 5.0%, MI 4.2%, CABG 3.0%, PTCA 4.2%, cardiac hospitalizations 17.2% (mean number 1.5 and duration 5.5 days). By 12 mos, 22.8% of pts had undergone additional hrs of EECP treatment.

Conclusions: In a cohort of high risk cardiac pts, EECP produced immediate and sustained improvement in CCS angina class in the majority of pts with MACE comparable to historical treatment trials.

EECP effect on CCS Angina Class

Angina Class	Baseline	Immediate Post EECP	6 Mos Post EECP	12 Mos Post EECP
No	0 %	17.6 %	27.8 %	34.1 %
I	6.4 %	33.7 %	33.7 %	24.7 %
II	27.2 %	30.8 %	24.1 %	24.5 %
III	46.9 %	12.7 %	9.9 %	12.2 %
IV	19.5 %	5.3 %	4.6 %	4.4 %

1117-76 Intervention for Stable Angina: A Multicenter Comparison of Consecutive Patients Undergoing Enhanced External Counterpulsation (EECP) and PCI

Richard Holubkov, Elizabeth D. Kennard, Sheryl F. Kelsey, Ozlem Soran, David R. Holmes, Jr.. *University of Pittsburgh, Pittsburgh, PA, Mayo Clinic Foundation, Rochester, MN*

Background: Many patients with CAD and stable symptoms who are treated with EECP are also suitable for percutaneous coronary intervention (PCI). Assessment of EECP outcome in these pts requires comparison of risk profile as well as follow-up status to patients with comparable symptoms who undergo PCI.

Methods: We compared baseline presentation and one-year outcome in two international multicenter cohorts of consecutive pts with stable angina: 148 PCI candidates undergoing EECP (International EECP Registry) and 411 pts undergoing nonemergent PCI in the NHLBI Dynamic Registry.

Results: PCI candidates undergoing EECP were older with more previous intervention and higher risk profile:

Baseline Presentation

	EECP (n=148)	PCI (n=411)
Mean age **	65.8 yrs	62.4 yrs
Female **	18%	30%
Prior PCI ***	60%	31%
Prior CABG ***	38%	15%
Prior myocardial infarction ***	57%	13%
History of congestive heart failure **	17%	8%
History of diabetes ***	43%	22%
Baseline angina severity: CCSC I/II/III/IV (%) **	13/30/39/18	5/45/45/5

**p<.01, **p<0.001.

At one-year follow-up, mortality was comparable (2.1% EECP vs. 2.2% PCI) as were rates of subsequent CABG (5.2% EECP vs. 5.1% PCI). During follow-up, 9.6% of those initially undergoing EECP had repeat course(s) of EECP, while 5.3% had subsequent PCI. Of the patients initially undergoing PCI, 17.0% underwent repeat PCI during follow-up. Angina was reported at one year in 60% of EECP pts vs. 26% of the PCI cohort (p<0.001). However, reported rates of severe angina (Class III, IV, or unstable symptoms) were 11% among EECP pts and 8% among PCI pts (p=ns).

Conclusions: PCI candidates undergoing EECP for stable symptoms have a markedly higher risk profile than patients with stable angina who undergo PCI. While angina is substantially more prevalent one year post EECP, more severe symptoms are reported relatively infrequently with each of the two treatments.

1117-101 Enhanced External Counterpulsation for Chronic Angina Is Associated With Improved Outcome at 6 Months

Gregory W. Barsness, Theresa Schnell, David R. Holmes, Jr.. *Mayo Clinic, Rochester, MN*

Background: There is a growing population of patients with severe ischemic chest pain (CP) who are not amenable to traditional revascularization strategies. EECP is a non-invasive, outpatient treatment that promotes diastolic augmentation and may reduce angina symptoms. **Methods:** 35 patients with severe angina (CCS angina class 3 or 4) despite optimal medical therapy underwent 35 one-hr EECP treatments over a 7-week period. Clinical characteristics, symptoms and follow-up events were recorded at baseline, at the end of treatment, and at 3, 6 and 12 months. The DASI score, a prospectively validated, semiquantitative assessment of cardiovascular functional status, was also measured via a self-administered questionaire. **Results:** Patients were elderly (median 69 yrs), primarily men (83%), with a history of diabetes (31%), hypertension (76%), tobacco use(67%), heart failure (16%), MI (48%), PCI (69%) and CABG (92%). 4 patients had prior TMR (3) or heart transplantation (1). Adverse treatment effects included local skin irritation in 2 patients. Angina measures improved during treatment with persistent benefit to 6 months (below). Throughout treatment and follow-up there were 13 clinical events, including 4 CP hospitalizations without MI, 2 NQWMI, 1 CHF, 5 PCI and 1 CVA, but no deaths.

Median (25,75)	Pre-EECP	Post-EECP	6-month	p (6-month)
Angina Class (CCS)	3(3,4)	2(2,2)	2(1,2)	<0.0001
#CP/wk	10(2.8,16.3)	2(0,3)	2(0,5)	0.0002
#NTG/wk	3(1,10)	0(0,2)	0.5(0,4)	0.009
DASI Score	7.2(4.5,13.5)	15.2(10.0,27.2)	18.8(10.5,26.8)	0.003

Conclusions: Non-invasive EECP treatment was associated with significant improvement in angina and functional status with few adverse effects in this high-risk cohort. These benefits were maintained at 6 months. Clinical event rates remain low through 6 months. Further evaluation of mechanism and longer-term durability of effect are warranted.

1117-102 Spinal Cord Stimulation for Refractory Angina Pectoris Patients: Data on Clinical Outcome From the Prospective Italian Registry

F Di Pede, G Zuin, S Greco, D Rapati, M Romanò, G Neri, A Circo, A Capucci, G Lanza, P Stritoni, GM Actis Dato, E Marangoni, M Maritano, M Barbiero, G Dragagno. *Cardiology Dept, Mestre-Venice, Italy*

The Prospective Italian Registry of Spinal Cord Stimulation [SCS] for severe refractory angina was designed to evaluate the immediate and long term clinical outcome of patients treated with SCS. From May 1998 to April 2000 87 patients (62 male, mean age 69 yrs) were implanted in 15 centers with an Itrel III Medtronic device. All pts implanted were followed up after 1-3-6-12 months. **Results:** Baseline clinical characteristics: diabetes 24%, hypertension 47%, dislipidemia 54%, CAD family hystory 24%, smokers 34%, mean duration of angina 7.6 yrs, CCS II 15%, CCS III 27%, CCS IV 58%, previous myocardial infarction [MI] 66%, CABG 47%, PTCA 37%, mean EF 0.48, triple vessel disease 82%. Stimulation was bipolar in 80% and continuous in 88% of pts. The mean follow up duration was 7.2 months. Complications: pocket infections in 5 pts, lead dislocation in 1 pt. Clinical events during follow up: MI in 1 pt, non sudden cardiac death in 3 pts, sudden death in 2 pts, non cardiac death in 2 pts. The CCS improved from a mean value of 3.39 ± 0.7 to 1.84 ± 0.7, the mean number of rest anginal attacks/week decreased from 5.3 ± 4.7 to 0.4 ± 0.7, the mean number of effort anginal attacks/week decreased from 4.5 ± 3.8 to 1.1 ± 1.1 and the mean number of dose nitrate consumption/week decreased from 8.6 ± 7 to 1.3 ± 1 after 12 months. Eighty-four percent of pts experienced more than 30% reduction of the number of anginal attacks and 51% had at least 2 CCS reduction. The need of hospitalization was analyzed in 47 pts with minimum period of 6 month follow up:

the number of patients admitted to the hospital for angina decreased from 35 (75%), during the 6 months period before SCS, to 8 (17%) during the 6 months period after SCS; in consequence the mean number of days in hospital per patient decreased from 21.5 ± 3.2 to 3.2 ± 5.5. **Conclusion.** SCS seems useful in reducing the number of anginal attacks, the nitrate consumption and the rate of hospital admission.

POSTER SESSION

1118 Measurement of Infarct Size and Myocardial Protection

Monday, March 19, 2001, Noon-2:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 1:00 p.m.-2:00 p.m.

1118-77 Sonomicrometry Myocardial Tagging Quantifies Regional Remodeling After Anteroapical Infarction

Benjamin M. Jackson, Robert C. Gorman, Joseph H. Gorman, III, T. Sloane Guy, IV, Sina L. Moainie, Theodore Plappert, Martin St.John-Sutton, L. Henry Edmunds, Jr.. *University of Pennsylvania School of Medicine, Philadelphia, PA*

Background: The relative contributions of infarcted, borderzone (normally perfused but hypocontractile), and remote myocardium to chronic left ventricular (LV) remodeling after myocardial infarction (MI) are uncertain. Echocardiography and MRI cannot quantify regional dilatation because they depend on anatomic landmarks susceptible to distortion with remodeling. We used sonomicrometry array localization (SAL), which allows identification of discrete locations within the myocardium throughout the remodeling process, to assess regional remodeling after anteroapical MI. **Methods:** Anteroapical infarctions were performed in 6 sheep with placement of 16 epicardial SAL piezoelectric transducers. At baseline (pre-infarction) and 30 min., 2, 5, & 8 weeks post-infarction, end-systolic chord lengths between SAL transducers were measured. Borderzone was assumed to be myocardium immediately adjacent to the infarct zone (but perfused) which did not contract after infarction (as measured by SAL). **Results:** At 30 min, the infarct dilated significantly, the borderzone slightly, and the remote segments did not dilate. From 30 min to 8 weeks, however, all regions dilated at approximately the same rate. % Expansion Relative to Baseline Segment Length Region 30 min 2 weeks 5 weeks 8 weeks Net (8 wks) Infarct 27±6 * 11±6 † 6±4 10±9 54±11 * Borderzone 7±6 * 8±4 7±5 10±5 † 32±5 * Remote 0±2 * 6±2 8±3 5±4 19±4 * * Significant difference between all pairs of groups (p<.05). † Significant difference between indicated group and "Remote" at same time point (p<.05). **Conclusions:** These data show that while early LV dilatation in anteroapical MI is predominantly due to infarct expansion, chronic remodeling is the result of balanced dilatation in all LV regions, including contractile segments. These results imply that mechanical stress is increased throughout the LV. The various determinants of wall stress likely act to differing degrees in each region. In the infarct, decreased wall thickness increases stress; in the borderzone, geometric changes (increased endocardial radius of curvature) increase stress; in remote myocardium, series contractile resistance increases stress.

1118-78 Endocardial Mapping Accurately Predicts the Transmural Extent of Myocardial Infarction

Tamir Wolf, Lior Gepstein, Gal Hayam, Rona Shofti, Asaph Zaretzky, Gideon Uretzky, Uri Oron, Shlomo A. Ben-Haim. *Cardiovascular System Laboratory, The Bruce Rappaport Faculty of Medicine, The Technion-I.I.T., Haifa, Israel*

Background: The degree of infarct transmural extent has previously been linked to patient prognosis and may have significant impact on therapeutic strategies. We hypothesized that catheter based mapping of infarcted tissue, and interpretation of endocardial electrophysiological information, is capable of delineating infarcts of various transmural subtypes.

Methods: In 13 dogs, electromechanical mapping was performed 4 weeks following LAD ligation, enabling a 3D reconstruction of the LV chamber. A concomitant reduction in bipolar electrogram amplitude (BEA) and local shortening (LS) indicated the infarcted region. In addition, impedance, unipolar electrogram amplitude (UEA) and slew rate (SR) were quantified. Subsequently, the hearts were excised; TTC stained, and sliced transversely. The mean transmural extent of the necrotic tissue in each slice was determined and infarcts were divided into (1) <30%; (2) 31-60%; and (3) 61-100% transmural subtypes to be correlated with the corresponding electrical data.

Results: All four indices delineated infarcted tissue. However, BEA (2.1±0.5mV, 1.2±0.2mV, 0.8±0.1mV in the three groups respectively, $P<0.05$ between each group) and SR (1.5±0.5mV/msec, 0.9±0.2mV/msec, 0.7±0.1mV/msec in the three groups respectively, $P<0.05$ between each group) proved superior to both UEA and impedance which could only differentiate between the first (<30%) and third (61-100%) transmurality subgroups.

Conclusions: The degree of infarct transmural extent can be derived from the endocardial properties of the tissue using electromechanical mapping. Utilization of such information may be helpful in determining the therapeutic approach and prognosis of patients suffering from myocardial infarction.

1118-79 Cardioproterction After Experimental Myocardial Infarction in Stroke-Prone Spontaneously Hypertensive Rats. Comparison Between Antihypertensive Treatment With ACE-Inhibitor, AT1-Receptor Antagonist and Combination Therapy

Alexander Reinecke, Marc Dorenkamp, Quingui Xia, Harro Bitterling, Susanne Penz, Christian Storz, Rüdiger W.R. Simon and Thomas Unger. *Institute of Pharmacology, University of Kiel, Kiel, Germany, Clinic of Cardiology, University of Kiel, Kiel*

Background: We compared the cardioprotective effects of the ACE inhibitor, fosinopril (Fos), the ANGII AT1 receptor antagonist, irbesartan (Irb), and the combined therapy with both substances (Comb) after experimental myocardial infarction (MI) in male stroke-prone SHRs (SHRSP) (n=88-235). **Methods:** To obtain strictly comparable hemodynamic conditions, treatment was started with equipotent antihypertensive doses 4 wks. prior to induction of MI and continued up to 6 weeks post MI. Sham operated and placebo treated infarcted rats served as controls. We investigated mortality, survival in relation to infarct size (IS), mean IS, cardiac dimensions, hemodynamics and myocardial collagen content. **Results:** In all investigated parameters, Irb was highly significant superior to Fos or Comb. Under treatment with Irb, rats significantly showed the lowest mortality after MI and survived the largest MIs. Moreover, Irb improved dP/dtmax in infarcted rats to a 2.2 and 2.6 fold higher extent than with Comb or Fos, respectively ($p<0.001$). Furthermore, myocardial collagen content six wks. after MI was 1.5 fold lower under Irb treatment compared to Fos ($p<0.001$). Combination treatment exerted no synergistically beneficial effect compared to Irb as a single drug treatment. **Conclusion:** When applied at equally antihypertensive doses, the cardioprotective effects of the AT1 receptor antagonism were significantly diminished in all parameters investigated when combined with an ACE inhibitor. The superior cardioprotection of Irb could be explained by its lack of kinin potentiation, second by lower myocardial catecholamine release and third by lower incidence of fatal arrhythmias after MI.

1118-80 Biosense NOGA Mapping for Detection of Myocardial Ischemia: Comprehensive Assessment in 74 Pigs

Gilbert P. Beran, Mark Post, Michael Simons, Dietmar Glogar, Roger J. Laham. *BIDMC/ Harvard medical School, Boston, MA*

Introduction: Biosense NOGA-mapping has been used to detect myocardial ischemia. This, however, is based on older software versions, small series, and limited experimental studies. The purpose of this study was to comprehensively and systematically evaluates NOGA maps as a tool for myocardial ischemia detection. **Methods:** 87 normal and ischemic (3-4 weeks after placement of a 2.25-2.5 mm ameroid constrictor on the left circumflex artery, LCX) Yorkshire pigs, which underwent NOGA mapping, were considered for the study. Angiograms were analyzed in ischemic animals to document LCX-occlusion. NOGA maps on all animals were assessed quantitatively (data for each acquired point) and semiquantitatively (0-6 scale) for linear local shortening (LLS, regional myocardial function) and unipolar (UPV) and bipolar (BPV) voltage. **Results:** 74 animals had maps and coronary status adequate for analysis [38 ischemic pigs and 36 non-ischemic animals]. By semi-quantitative analysis, with moderate to severe (grade 3-6) impairment in LLS as a cutoff for ischemia, sensitivity of NOGA mapping was 82% and specificity was 61% (positive predictive value: 68%; negative predictive value: 76%). In the quantitative analysis, 5423 points (72.4±14.4 per animal) were measured. Given species differences, the rotational angle (theta) was shifted 40° clockwise to adjust for anatomical position. UPV and BPV were preserved in both normal and ischemic animals. LLS, however was impaired in the lateral wall of ischemic compared to normal pigs [8.9%±1.40 (SE) vs. 11.2%±1.44, $p<0.001$). Ischemic animals had lower LLS in the mid (8.4%±1.60 vs. 11.6%±1.59 $p<0.001$) and basal (8.3%±1.44 vs. 10.7%±1.34, $p<0.005$) but not in the apical lateral wall ($p=0.14$). Interestingly, LLS of the septal wall was higher in ischemic than normal animals (12.0%±1.44 vs. 10.1%±1.34, $p<0.005$), possibly secondary to compensatory hypercontractility. There was a good correlation between semi-quantitative and quantitative analysis ($r=0.81$; $p< 0.001$). **Conclusion:** NOGA mapping in this large study can detect ischemia with reasonable accuracy. The average LLS in ischemic myocardium of 8.4% warrants increasing the detection threshold for clinical NOGA maps.

1118-81 No Impact of an AGE-Crosslink Cleaving Agent Found in Rat LV Infarct

Paul S. Hees, David E. Bush, Michelle H. Leppo, Edward P. Shapiro. *Johns Hopkins University, Baltimore, MD*

Background

The advanced glycation endproduct (AGE)-crosslink cleaving agent ALT-711 reduces vascular stiffness in animal models, and is currently being studied in humans. However, the 'de-stiffening' effect of the drug could reduce scar formation and promote infarct (MI) expansion, a deleterious effect. Alternatively, new evidence suggests that the drug also mutes the proliferative response to myocardial overload, ie, has a neuro-hormonal effect analogous to that of ACE inhibition, which might improve post-MI remodeling. We therefore studied post MI remodeling following ALT-711 in a rat model of MI.

Methods

Treated animals (n=14) received ALT-711 (10 mg/kg/da IP) for 1 mo prior to infarct, while 15 controls received placebos. Animals underwent thoracotomy and LAD ligation. Ischemia was confirmed by visual observation of blanching in the LAD bed and ST elevation. The chest was closed and the animal recovered, continuing ALT-711. Animals were sacrificed 2 wk after MI, and the hearts fixed at end-diastole, sectioned, and examined histologically to assess morphology after expansion.

Results

Results tabulated for 9 ALT-711's and 8 controls surviving MI and post-MI period.

Conclusions

ALT-711 had neither a deleterious nor beneficial effect on post-MI remodeling, with no evidence for an alteration in infarct expansion, wall thinning, or hypertrophy. A trend toward reduced infarct size (MI) and wall thickness in the remote zone (LVWT) with ALT-711 requires continuing study.

Morphometric Results in Treated and Control Rats Following Infarct

	BW,g	LVM/BSA, g/kg	LVV/BW, cc/kg	MI,g	MI%	MIWT, mm	LVWT, mm
ALT-711	321±29	1.43±.34	.28±.08	.11±.05	25±9	1.65±.45	2.56±.22
Control	357±42	1.55±.21	.29±.06	.16±.04	30±7	1.60±.31	2.72±.13
p-value	0.05	0.41	0.94	0.04	0.22	0.78	0.09

BW=Body weight; LVM=LV mass; LVV=LV cavity volume; MI=mass of infarcted zone; MI%=100*MI/LVM; MIWT=wall thickness in MI zone; LVWT=remote zone WT

1118-82 Apstatin, a New Inhibitor of Aminopeptidase P, Reduces Myocardial Infarct Size by a Kinin-Dependent Pathway

Sebastian Wolfrum, Andreas Dendorfer, Klaus Tempel, Gert Richardt. *Medical Clinic II, University of Lübeck, Lübeck, Germany, Institute of exp. and clin. Pharmacology and Toxicology, University of Lübeck, Lübeck, Germany*

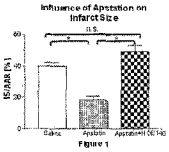


Figure 1

Background: Inhibitors of the angiotensin converting enzyme (ACE) have been shown to exert their cardioprotective actions through a kinin-dependent mechanisms. ACE is not the only kinin degrading enzyme in the rat heart. Since aminopeptidase P (APP) has been shown to participate in myocardial kinin metabolism to the same extent as ACE, in the present study we investigated whether inhibition of APP by its specific inhibitor apstatin leads to a reduction in myocardial infarct size after acute ischemia and reperfusion. **Methods:** Anesthetized, open-chest rats were instrumented for measurement of systemic hemodynamics. Animals were subjected to 30-min left main coronary artery occlusion followed by 3-h reperfusion. Apstatin (1 mg/kg), a selective inhibitor of APP or saline were administered 5min before ischemia, and rats receiving HOE 140 (0.5 mg/kg), a specific bradykinin-B(2)-receptor-antagonist, were pretreated 2min prior to apstatin. After reperfusion, myocardial infarct size (IS) was determined by tetrazolium staining and expressed as a percentage of area at risk (AR). **Results:** As given in figure 1, IS/AR% was significantly reduced in rats that received apstatin (18 +/- 2%, $p < 0.05$) as compared with those receiving saline (40 +/- 2%) or apstatin plus HOE 140 (49 +/- 4%). **Conclusion:** Apstatin reduces infarct size in an in vivo model of acute myocardial ischemia and reperfusion. Cardioprotection achieved by the new inhibitor of Aminopeptidase P is mediated by bradykinin. Inhibion of other kininases than ACE could therefore open additional therapeutic strategies for the treatment of acute myocardial infarction.

1118-83 Na+/H+ Exchange Inhibition Protects Ischemic Myocardium Independent of Potassium-ATP-Channels

Marie-Luise von Brühl, Claudia Strohm, Wolfgang Schaper. *Department of Experimental Cardiology, Max-Planck-Institute for Physiological and Clinical Research, Bad Nauheim, Germany*

Background: It has been shown that several Na^+/H^+ exchange (NHE) inhibitors protect against myocardial injury following ischemia/reperfusion. We investigated the role of ATP sensitive potassium (K_{ATP}) channels and of the p38-mitogen activated protein kinase (MAPK) in cardioprotection induced by BIIB722Cl, a new NHE inhibitor in a porcine model of myocardial ischemia and reperfusion. We have reported that BIIB significantly reduced infarct size (IS = infarct area / risk area) in ischemia (coronary occlusion) followed by reperfusion. We now investigated, whether the cardioprotective effect of BIIB is preserved during K_{ATP}-channel blockade by glibenclamide.

Methods: Landrace pigs were treated with BIIB prior to left anterior descending artery (LAD) occlusion. BIIB (in NaCl/DMSO) was administered either intravenously at a dose of 1.5 mg/kg (n=4, group A) or 3 mg/kg (n=5, group B) for 15 min. The control group received only the solvent. BIIB was also given via intramyocardial (50mM in NaCl/DMSO) microinfusions into the prospective area at risk for 60 min (n=3, group C). For group D the protocol of group C was used with the simultaneous systemic application of glibenclamide (0.5mg/kg) (n=3). In all animals the LAD was occluded for 60 minutes followed by 60 minutes of reperfusion. The amount of dual-phosphorylated p38-MAPK (Thr180/Tyr182) was measured by Western blot analysis at various timepoints of ischemia.

Results: Treatment with BIIB significantly decreased IS ($P<0.05$) in group A and B when compared to the control group (35.4±3.9%, 40±7.5%, 62.2±6.% , respectively). In group C and D a marked myocardial protection was shown by the presence of viable (triphenyltetrazolium chloride stained) myocardium around microinfusion needles delivering BIIB that was not seen around needles with solvent. Treatment with BIIB was associated with a decrease of phospho-p38-MAPK.

Conclusion: The preservation of the protective effect of BIIB722CL in the presence of glibenclamide suggests a survival pathway independent from the K_{ATP}-pathway but may be mediated by its effect on the p38-MAPK signal transduction pathway.

POSTER SESSION

1119 Surgical Strategies for Patients With Heart Failure

Monday, March 19, 2001, Noon-2:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 1:00 p.m.-2:00 p.m.

1119-84 Hybrid Gene Therapy in Patients Turned Down for Coronary Bypass Surgery: an Option for No Option Patients?

S Kassam, M Kutryk, A Campbell, N Camack, D Latter, L Erret, R Chisholm, D Fitchett, D J. Stewart. *St Michael's Hospital, Toronto, Canada*

A significant proportion of patients with severe symptomatic coronary artery disease are considered unsuitable for either coronary bypass grafting (CABG) or percutaneous coronary intervention (PCI), and many are being referred for non-conventional revascularization procedures, including gene therapy. We describe the initial experience of a newly established gene therapy program for myocardial angiogenesis. From January to August 2000, 127 patients with severe angina, considered to be unsuitable for CABG or PTCA were evaluated by a team of interventional cardiologists and cardiac surgeons. In 19 (15%), a standard revascularization procedure was recommended (12 CABG; 7 PCI). In this group, there was an operative mortality of 8% (1/12). 96 patients were found to be ineligible for the clinical trials: CCS angina class <3, 29; LVEF < 25%, 16; LBBB, 12; ischemia-symptom mismatch, 8; history of or active malignancy, 7; miscellaneous reasons, 24. After successful screening, 12 patients (10%) were entered into a trial. 6 had CABG with adjuvant intramyocardial plasmid DNA for VEGF165, 2 were given plasmid DNA for VEGF165 with the Biosense NOGA needle injection catheter delivery system and 4 were randomized into controlled trial (2 assigned to active treatment with adenoviral VEGF121 via minithoracotomy). All patients survived to 90 days post procedure. Of the 10 patients treated with VEGF165 gene therapy + CABG, the mean CCS class was reduced from 3.56 + 0.50 to 0.88 + 0.83 ($p<0.0001$) and mean global perfusion score in segments receiving VEGF was improved from 8.00 + 4.00 to 4.13 + 3.36 segments ($p<0.01$). Therefore, we conclude that only a small proportion of patients referred for myocardial angiogenesis with "inoperable" coronary disease are suitable candidates for VEGF gene therapy. However in this observational study these patients appear to benefit.

1119-85 Surgical Reconstruction of the Left Ventricle (Dor Procedure) in Postinfarction Patients With Moderate to Severe Congestive Heart Failure: An Observational Study

Marisa Di Donato, Anna Toso, Michel Sabatier, Vincent Dor, Mauro Maioli, Gian Franco Gensini, Gerald Buckberg. *Dpt of Critical Care Medicine, Florence, Italy, CardioThoracic Center, Monaco, Monaco*

Background: The long term effects of surgical reconstruction of the left ventricle (Dor procedure) in postinfarction patients with heart failure are only partially known, yet. **Methods:** The study reports early and late results in 179 consecutive patients (59±9yr) operated by Dor procedure at the Cardiothoracic Center of Monaco, retrospectively selected if they had EF<40% and NYHA class II and III. Hemodynamic study before and early after surgery was performed in all pts;1 year study was done in 94 pts. **Results:** There were 114 dyskinetic and 65 akinetic scar. Delay from myocardial infarction was 52±66 months. Clinical signs of cardiac failure were present in 133. Urgent operation was performed in 17. The extent of non contractile myocardium was 58±14 % of the LV perimeter. Mild to moderate mitral regurgitation was present in 40. Associate procedures were: CABG in all, mitral repair in 12, replacement in 6 and aortic replacement in 2. Perioperative mortality rate was 5.6% (10/179). Two were transplanted in the perioperative period. Mean follow-up was 40±20 months; there were 19 late deaths; 2 patients were transplanted (1 died 1 year after) and 4 were in a transplant list. The table shows hemodynamic data before and after surgery (*vs basal; # vs early postop). **Conclusion:** In pts with postinfarction large ventricular volumes, depressed ventricular function, and moderate to severe clinical status Dor procedure has an acceptable operative risk, improves functional class and pump function and has a favorable impact on late survival (89% of surviving patients and 83% of the overall population, are alive during our observational period). A randomized trial is needed to confirm our results in a larger population and at different Institutions.

	EDVI ml/m2	ESVI ml/m2	EF %	CWP ml/m2	CI L/min/m2	NYHA
PREOP	183±86	131±65	29±7	16±7	2.6±.7	2.6±.5
EARLY POSTOP	98±43*	55±30*	45±11*	11±7*	2.6±.6	
1 YEAR	122±49*#	71±32*#	42±11*	18±10#	2.7±.6	1.5±.7*

1119-86 Real-Time Three-Dimensional Echocardiographic Follow-Up of Patients With Ischemic Cardiomyopathy Undergoing Infarct Exclusion Surgery

Jian Xin Qin, Takahiro Shiota, Patrick M. McCarthy, Neil L. Greenberg, Fabrice Bauer, Marta Sitges, Jeanne K. Drinko, Xi-Yi Hang, Yong Jin Kim, Kathy J. Hoercher, Tiffany Buda, Nicholas G. Smedira, James D. Thomas. *The Cleveland Clinic Foundation, Cleveland, OH*

Background: We have previously shown the immediate efficacy of infarct exclusion surgery (IE) for reducing left ventricular (LV) volumes and increasing ejection fraction (EF) in patients with ischemic cardiomyopathy using real-time three-dimensional echocardiography (RT3DE). The purpose of this study was to evaluate whether this benefit persists after the surgery during a mid-range follow-up.
Methods: Forty-six patients (mean age 63 ± 9 yr) who had undergone IE surgery were studied. The surgical procedures included infarct exclusion, coronary bypass and mitral valve repair (23 patients) when associated with significant mitral regurgitation (MR). Transthoracic RT3DE was performed before IE, before discharge (average 7±4 days after IE) and during follow-up (average 9±2 months). The LV volumes were determined using multi-parallel 7-11 short axis planes with Simpson's method.
Results: No significant MR was found after the IE surgery. LV end-diastolic (EDV) and end-systolic (ESV) volumes were significantly decreased and LV EF (EF = (EDV – ESV)/ EDV × 100) and forward stroke volume (FSV) (FSV = EDV-ESV-MR volume) significantly increased before the discharge after the IE surgery. At the average 9-month follow-up, LV EF and FSV remained higher than before IE. LV volumes remained lower (164 ± 56 ml for EDV and 97 ± 48 ml for ESV, both $p > 0.05$) in 38 patients, but 8 patients showed recovered LV dilation (> 50% in comparison with that before discharge) (Table).

	EDV (ml)	ESV (ml)	FSV (ml)	EF (%)
Before IE	227 ± 82	162 ± 66	22 ± 12	29 ± 10
Discharge	152 ± 57*	94 ± 46*	58 ± 20*	40 ± 9*
9-month	183 ± 64#	103 ± 46#	79 ± 35#	43 ± 12

* vs before IE, $p < 0.001$; # vs before discharge, $p < 0.05$.
Conclusion: RT3DE demonstrated sustained benefit in LV ejection fraction and forward stroke volume in patients undergoing IEsurgery after a follow-up of 9 months.

1119-87 Beta-Blocker Attenuates the Development of Intramural Small Coronary Vessel Disease in Chronic Hibernating Myocardium Subtending a Severe Epicardial Coronary Stenosis

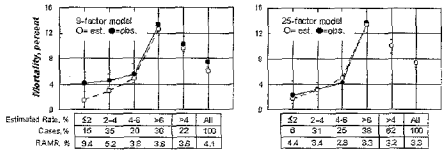
Huashan Hong, Seigei Aksenov, Joseph Marak, John Fallon, David Waters, Chunguang Chen.. *Newark Beth Israel Medical Center, Newark*

Recovery of LV dysfunction after revascularization is often both incomplete and delayed in hibernating myocardium. We have previously shown that chronic myocardial ischemia induces significant wall thickening of intramural small coronary vessels with reduced lumens, preventing complete restoration of myocardial perfusion/flow reserve after revascularization. To test the hypothesis that a beta-blocker attenuates wall thickening and lumen narrowing of small vessels distal to epicardial coronary stenosis (CS), we studied 21 pigs in 3 groups: Group 1: 9 pigs with 4-week severe proximal LAD CS to reduce coronary flow (CF) by ~30% with LV dysfunction; Group 2: 6 pigs with severe CS as in Group 1 + metoprolol (100 mg x 2 /day) for 4-weeks; Group 3: 6 pigs as controls. CF reduction(%) by implanted flowmeter, LV ejection fraction (EF,%) and LV wall thickening (WTm,%) were monitored. Quantitative microscopic study of arterial wall thickness (WTa), lumen diameter (LDa) and WT/LDa ratio of small coronary vessel (30-90 um) and myocardial fibrosis were performed. **Results:** CF (33+/-6% reduction), WTm (12+/-5%) and LV EF (37+/-7%) were significantly reduced in Groups 1 and 2 compared to control Group 3 ($p<0.01$). Significant wall thickening of small intramural vessels with reduced luminal diameters was found in Group 1 (WTa=17.2+/-3.2 um, WTa/LDa=1.34+/-0.15) and in Group 2 (WTa=13.3+/-1.5 um, WTa/LDa=0.38+/-0.03) compared to controls (WTa=9.8+/-2.5 um, WTa/LDa=0.34+/-0.03,both $p<0.05$). Metoprolol significantly reduced WTa with increased LDa in Group 2 compared to Group 1(both $p<0.01$). **Conclusion:** Chronic myocardial ischemia induces significant arterial wall thickening with reduced vessel lumens in small intramural coronary vessels. Beta-blocker significantly attenuates, but did not completely prevent, the development of this small vessel disease in chronic ischemic, hibernating myocardium distal to epicardial coronary stenosis. Thus, the preoperative administration of a beta-blocker may enhance the improvement of myocardial perfusion/flow reserve after revascularization via this mechanism.

1119-88 Relative Advantage of a Comprehensive Logistic-Regression Model for Preoperative Estimation of the Risk of Aortocoronary-Bypass Surgery

Alan D. Bernstein, Victor Parsonnet. *Newark Beth Israel Medical Center, Newark, NJ*

Background. Risk-adjusted outcome evaluation of aortocoronary-bypass surgery is an important resource for assessing the quality of care at regional, hospital, and surgeon levels, and in discussions with patients who are considering surgery as a possible therapeutic option. Several existing logistic-regression models used for this purpose incorporate only a limited number of preoperative risk factors, excluding (and treating as absent) many factors that in individual patients may increase the likelihood of operative mortality. **Methods.** We developed a logistic-regression model (ROC area 0.792) comprising 25 distinct risk factors and 30 covariates from data encompassing 16,246 isolated aortocoronary-bypass procedures performed at 13 New Jersey hospitals in 1996 and 1997. This model, in which more liberal standards of statistical significance were accepted, was compared with a previously published 9-factor, 13-covariate model (ROC area 0.781) derived from an earlier version of the same dataset. **Results.** Risk-adjusted mortality rates (RAMRs) derived from the comprehensive model were more consistent with observed mortality rates. In contrast, the 9-factor model underestimated the operative risk seriously in half of the 30% of patients with >4 risk factors (see plots), giving those 2,408 patients an erroneously inflated and potentially misleading RAMR (5.91%, vs. 3.56% with the 25-factor model). **Conclusions.** A risk-estimation model that incorporates many objective, reliably determined risk factors affords risk stratification that is fairer and closer to reality than a more limited model can provide. The limited model was specifically detrimental to surgeons who treated many high-risk patients. RAMRs calculated using a more complete model do not penalize hospitals or surgeons that accept high-risk patients.



POSTER SESSION

1120 General Clinical Risk Markers in Acute Coronary Syndromes

Monday, March 19, 2001, Noon-2:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 1:00 p.m.-2:00 p.m.

1120-89 Clinical Risk Stratification Predicts Extent of Coronary Artery Disease in Patients With Unstable Angina

Verghese Mathew, Michael E. Farkouh, Lynn Urban, Diane Grill, David R. Holmes, Jr., Bernard Gersh. *Mayo Clinic, Rochester, MN*

Background: The Agency for Health Care Policy and Research (AHCPR) guidelines for unstable angina stratify patients into low, intermediate, and high risk subgroups according to the short-term risk of death or myocardial infarction (MI). Whether these guidelines are useful in predicting the severity of coronary artery disease by angiography is unknown.
Methods: From 1985-1992, 892 patients in the Olmsted County Acute Chest Pain Study with unstable angina underwent angiography within 7 days of index presentation; 64 (7.2%) were low risk, 641 (71.9%) intermediate risk, and 187 (21%) high risk patients according to AHCPR criteria.
Results: Normal or mild disease (<50% stenosis) was more likely in low risk patients, relative to both high risk (OR 13.6, 95% CI 6.9-26.8) and intermediate risk patients (OR 5.4, 95% CI 3.1-9.4). Significant 1,2,3 vessel (≥70% stenosis) or left main (≥50% stenosis) disease was more common in high-risk patients relative to low (OR 9.9, 95% CI 5.2-19), and in intermediate relative to low risk patients (OR 4.9, 95% CI 2.8-8.5). Three vessel or left main disease was common in high relative to intermediate risk patients (OR 1.5, 95% CI 1.03-2.2) and in high relative to low risk patients (OR 11, 95% CI 2.6-47.7).
Conclusion: Among patients with unstable angina undergoing coronary angiography within 7 days of presentation, short-term risk stratification according to AHCPR guidelines correlates with the angiographic extent of coronary artery disease.

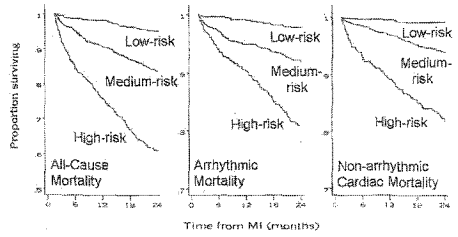
1120-90 Risk Stratification in Patients After Myocardial Infarction Using Demographic Risk Factors: A Powerful Prognostic Indicator

Yee Guan Yap, Trinh Duong, Martin Bland, Marek Malik, Christian Torp-Pederson, Lars Kober, Stuart Connolly, Robin Roberts, Bradley Marchant, A. John Camm. *St. George's Hospital Medical School, London, United Kingdom*

Background: Risk stratification of patients after myocardial infarction (MI) at high risk of mortality remains expensive and disappointing. Demographic features may provide useful prediction but contemporary information is lacking on their effect on the specific mode of mortality after MI in the thrombolytic era. We report the clinical value of a powerful prognostic indicator using demographic information. **Method:** We combined individual patient data from the placebo arms of EMIAT, CAMIAT, TRACE & DIAMOND-MI with LVEF/= 45 days after MI. Risk factors for mortality up to 2-years were examined (Cox regression). Risk scores were derived from the equation of a Cox regression model containing only the significant variables. The prognostic index was the sum of the individual contribution from their risk factors. **Result:** 2707 patients were pooled (age: 66(23-92) yr, 2132M) with 480 deaths at 2 yrs (213 arrhythmic & 171 cardiac deaths). Variables predicted mortality were age, sex, previous MI, previous angina, hypertension, diabetes, systolic blood pressure, heart rate & Q-wave. Distinct survival curves were obtained for 3 risk groups based on the median & inter-quartile range for the prognostic index (figure). In the high risk group, up to 40% of patients died of all-cause mortality and 33% died of arrhythmic and 32% died of cardiac mortality at 2-year. **Conclusion:** Our prognostic

index provides a simple powerful bedside risk stratification tool using baseline information for the prediction of various modes of mortality. Furthermore, we proposed that such information should be considered when designing risk stratification or survival studies.

Risk Score	Low risk	Medium risk	High risk
All-cause mortality	4.8	16.4	39.6
Arrhythmic mortality	2.2	8.1	19.1
Cardiac mortality	0.9	6.1	18.2



1120-91 Acute Myocardial Ischemia and Alternative Diagnoses in Low-Risk Patients for Coronary Event Presenting to the Emergency Department

Alberto Conti, Barbara Paladini, Maurizio Zanobetti, Stefano Grifoni, Stefania Sartini, Sabrina Masetti, Chiara Gallini, Paolo Ferri, Egidio Costanzo, Maria Matteini, Giacomo Trallori. *AZIENDA OSPEDALIERA CAREGGI, FIRENZE, Italy*

Background. The evaluation of patients with chest pain (CP) and non-diagnostic ECG doesn't generally go beyond the exclusion of acute coronary events. Thus, the underlying presence of depression and gastroesophageal disease is often neglected and of unknown proportions. In this study, we addressed this issue in a population of 214 consecutive patients presenting at the Emergency Department with chest (CP) pain and non diagnostic ECG. **Methods.** All patients had CP lasting >10 minutes within 24 hours before admission, and a negative first line evaluation based on serial ECGs, cardiac enzymes, echocardiography and chest X rays. Patients underwent rest-SPET (<3 hours from CP and exercise-SPET (>3 hours) followed by coronary angiography when positive. All patients without documented coronary artery disease, underwent: 1) psychiatric screening using the Hospital Anxiety and Depression Scale questionnaire (HADS); all patients with a HADS score >8 were submitted to psychiatric interview for final diagnosis, according to the Diagnostic and Statistical Manual IV; 2) gastroesophageal endoscopy. **Results.** Of the 214 patients, 27 patients (13%) had documented coronary artery disease and 74 patients (35%) had CP of parietal origin. Among the remaining 48% (n=113 patients), HADS > 8 was founded in 54 patients (25%) and depression or panic disorders were detected in 22 patients (10%). Gastroesophageal pathology was documented in 59 patients (27%; peptc ulcer and HLO in 17% and esophageal reflux in 10% of patients). **Conclusions**. In one half of patients with non-diagnostic ECG, chest pain was associated with psychiatric or gastroesophageal disorders that usually may be grossly underestimated in the emergency department. Detection of alternative diagnoses and correct related management for patients without coronary artery disease could reduce readmission visits at the Emergency Department.

1120-92 Predictors of Heart Failure Development After Non-ST Elevation Acute Coronary Syndromes

Eric J. Velazquez, Douglas A. Criger, David Hasdai, Robert M. Califf, Robert A. Harrington. *Duke University, Durham, NC*

Heart failure (HF)after ST-segment elevation acute myocardial infarction portends a worse prognosis. Most patients with an acute coronary syndrome (ACS) present without persistent ST elevation yet HF development in this broader patient group is poorly characterized. **Methods:** Patients in a large international trial of ACS without ST-segment elevation were categorized by the in-hospital development of HF or not. Univariable regression analysis was done on baseline factors and in-hospital and 180-day endpoints. A multivariable Cox proportional hazards model was built using variables found significant in the univariable analysis to determine which factors contributed to HF development. **Results:** Of the 9461 patients randomized to high-dose Eptifibatide or placebo in the PURSUIT trial, 495 patients (5.2%)had an episode of HF in the hosital. The following baseline variables, presented as odds ratios with 95% C.I., were related to in-hospital HF development: previous HF 2.49 (2.03-3.05), previous MI 1.42 (1.18-1.71), smoking 1.38 (1.14-1.69), hypertension 1.32 (1.09-1.61), diabetes mellitus 1.27 (1.05-1.47), age 1.06 (1.05-1.07), heart rate 1.02 (1.02-1.03), systolic blood pressure 0.99 (0.98-1.00), Eptifibatide therapy 0.93 (0.78-1.11), and previous percutaneous coronary intervention 0.62 (0.45-0.85). The mortality rate at 180 days after the ACS event was 39% in the HF group compared with 5% in the group without HF (p<0.001). **Conclusion:** HF develops in a minority of patients presenting with a non-ST elevation ACS but is predictive of a marked excess in 6-month mortality. Investigation of strategies that help identify this patient group for appropriate risk stratification and more aggressive therapies is warranted.

1120-93 Prognostic Significance of Conduction Disorders Complicating Acute Myocardial Infarction in the Elderly

Saif S. Rathore, Bernard J. Gersh, William J. Oetgen, Allen J. Solomon. *Georgetown University Medical Center, Washington, DC, Delmarva Foundation for Medical Care, Easton, MD*

Background: Although disorders of cardiac conduction are common in patients presenting with acute myocardial infarction (MI), patient characteristics and outcomes remain poorly defined in the elderly.
Methods: We evaluated 106,720 Medicare beneficiaries age 65 years and older who presented with MI between 1994 and 1996. Subjects who were not transferred during hospitalization with valid electrocardiographic data were evaluated to determine the presence of right bundle branch block (RBBB), left bundle branch block (LBBB), fascicular block (FAS), or bifascicular block (BIF) at time of admission. The influence of RBBB, LBBB, FAS, and BIF on mortality was evaluated by logistic regression modeling of 30-day mortality and Cox proportional hazards modeling of long-term mortality (mean follow-up=575 days).
Results: 22,181 (20.8%) subjects had a conduction disorder documented at admission: 7,678 (7.2%) presented with LBBB, 6,419 (6.0%) with RBBB, 5,428 (5.1%) with FAS, and 2,657 (2.5%) with BIF. Patients with conduction disorders had a higher crude in-hospital (LBBB 22.4%; RBBB 26.8%; BIF 24.6%; FAS 18.3%; no disorder 16.8%, p=0.001), 30-day (LBBB 26.7%; RBBB 30.0%; BIF 29.0%; FAS 22.2%; no disorder 19.9%, p=0.001), and one-year (LBBB 49.9%; RBBB 45.6%; BIF 46.8%; FAS 37.2%; no disorder 33.8%, p=0.001) mortality. Multivariable adjustment for patients' clinical and demographic characteristics confirmed higher risk of 30-day mortality among patients with LBBB (RR 1.08, 95% CI:1.03,1.13), RBBB (RR 1.28, 95% CI:1.22,1.34), and BIF (RR 1.23, 95% CI:1.15,1.32) block; FAS was not associated with increased mortality (RR 1.04, 95% CI:0.98,1.10). Similar findings were obtained for risk of long-term mortality among patients with LBBB (HR 1.25, 95% CI:1.22,1.29), RBBB (HR 1.24, 95% CI:1.20,1.29), and BIF (HR 1.24, 95% CI:1.18,1.30); FAS block had limited prognostic significance at long-term follow-up (HR 1.04, 95% CI:1.00,1.08).
Conclusion: Conduction disorders are a common complication of MI in elderly patients. Left bundle, right bundle, and bifascicular blocks are associated with increased short and long-term mortality, while a solitary fascicular block is not of prognostic significance.

1120-94 The Management and Investigation of Elderly Patients With Acute Coronary Syndromes Without ST Elevation: An Evidence-Based Approach? Results of the Prospective Registry of Acute Ischaemic Syndromes in the United Kingdom (PRAIS-UK)

Julian R. Collinson, Marcus D. Flather, Ameet Bakhai, Marcelo C. Shibata, Diego Perez, Erwin A. Rodrigues, Iain Findlay. *Royal Brompton and Harefield NHS Trust, London, United Kingdom*

Background: In the elderly, acute coronary syndromes (ACS) without ST elevation are a frequent and important cause of admission. In the United Kingdom, practice patterns and outcomes in these patients need to be assessed. **Methods:** We enrolled 1046 patients admitted with ACS without ST elevation to 56 UK centres (20 consecutive patients per centre) and followed them for 6 months. We compared baseline characteristics, outcomes and treatments in Group 1: those aged over 80 (n=119, 11%), Group 2: from 70 to 80 (n=301, 29%) with Group 3: those below 70 (n=572, 60%). **Results:** The proportion of males was 40%, 52%, and 69% respectively (p<0.001). There were no differences in the proportion of patients with diabetes (17% overall), treated hypertension (38%) or prior MI (48%). The proportion with ST depression or bundle branch block on the admission ECG were 40%, 39%, and 22% (p<0.001) respectively and a normal admission ECG was seen in 13%, 10%, and 19% (p<0.01) respectively. Median length of stay was 6, 5, and 4 days (p=0.03). The rate of the composite endpoint of death or new MI at 6 months was 13%, 18%, and 8% (p<0.001) respectively. Any heparin was used in 61%, 70%, and 75% (p<0.01) respectively and aspirin in-hospital in 83%, 84%, and 89% (p=0.03) respectively. Lipids were measured in 49%, 58%, and 68% (p<0.001) and total cholesterol found to be greater than 5.0 mmol/l (190 mg/dl) in 44%, 43% and, 41% (no difference). At 6 months, beta blockers were used in 29%, 38%, and 45% (p<0.001) and statins in 32%, 40%, and 55% (p<0.001) respectively. Rates of angiography were 18%, 21%, and 36% (p<0.001) and of revascularisation 9%, 12%, and 18% (p=0.01). In-hospital stress testing was performed in 2%, 9%, and 16% (p<0.001) respectively. **Conclusion:** In this large population based registry of UK patients admitted to hospital with ACS without ST elevation, those aged over 70 are at substantially higher risk of adverse events than younger patients. However, they are less likely to receive treatments of proven benefit or to be investigated with a view to revascularisation. A more aggressive approach to these patients is likely to result in substantial benefits.

POSTER SESSION

1121 Myocardial Perfusion During Acute Myocardial Infarction

Monday, March 19, 2001, Noon-2:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 1:00 p.m.-2:00 p.m.

1121-95 Kinetics of Myocardial Perfusion in the Setting of ST Segment Elevation Acute Myocardial Infarction vs Unstable Angina/Nonq-Wave MI

Matthew H. C. Otten, Sabina A. Murphy, Brad Angeja, Colin A. Hynes, Jessica S. Lim, Lily L. Luu, Sarah R. Kermgard, Susan J. Marble, Chistopher P. Cannon, Eugene Braunwald, C. Michael Gibson. *University of California, San Francisco, San Francisco, CA, Brigham and Women's, Boston, MA*

Background: The goal of this study was to compare the kinetics & appearance of myocardial perfusion (blush) in the setting of ST elevation myocardial infarction (STEMI) & Unstable Angina / non Q-Wave MI (UA). We hypothesized that dye filling of the myocardium would be delayed in patients with STEMI vs UA. **Methods:** STEMI data were obtained from 775 pts in the TIMI 10B trial comparing TNK vs. tPA & from 248 pts in the LIMIT trial comparing tPA+ rhuMab CD18 (a WBC antibody) vs tPA + placebo. UA data were drawn from TIMI 18 patients randomized to either conservative or invasive management of UA who underwent PCI or diagnostic angiography & had TIMI myocardial perfusion grade (TMPG) data available (n=560). Blush was assessed using the TMPG. Grade 1 TMPG is a stain of the myocardium (dye remains in the myocardium on the next injection). To assess the kinetics of blush, the number of frames required for blush to 1st appear & the number of frames for dye to reach peak intensity were counted & converted to 30 frames per second. The blush was characterized as heterogenous (patchy) or diffuse. **Results:** When adjusted for location of infarct, an increase of myocardial staining (TMPG 1) occurred in the setting of STEMI vs UA (O.R. of 2.6; p<0.001). After controlling for flow in the epicardial artery (Corrected TIMI frame count), the frame for 1st & peak appearance of blush both remained significantly slower in STEMI. **Conclusions:** A two-fold increase in both the incidences of myocardial staining (TMPG 1) & heterogenous, hyperintense regions of blush was observed in STEMI when compared to UA. It took longer for dye to reach the myocardium & to reach peak intensity, even when adjusting for epicardial flow. Thus, independent of impaired epicardial flow, perfusion of the myocardium is delayed in the setting of STEMI compared with UA. These results may explain in part the poorer early outcomes observed in this group of patients.

	UA/ Non Q-Wave MI	STEMI	p-value
% of pts w/ TMPG 1	5.92% n=31/560	11.04% n=111/1005	<0.001
Heterogenous Blush	13.8% n=66/479	22.6% n=43/190	0.005
Frame Blush 1st Appears	44.7 ± 26.5 n=540/560	51.1±25.7 n=184/248	0.0044
Frame for Peak Blush	104.6± 42.5 n=445/560	122.5 ± 44.4 n=187/248	<0.001

1121-96 The Kinetics of TIMI Myocardial Perfusion Grades 2 & 3 in the Setting of Acute MI: A LIMIT Substudy

Matthew H. C. Otten, Sabina A. Murphy, Brad Angeja, Lily L. Luu, Sarah R. Kermgard, Jessica S. Lim, Colin A. Hynes, Jen Kliris, Susan J. Marble, Kent Dauterman, Priscilla Hsue, C. Michael Gibson. *University of California, San Francisco, San Francisco, CA*

Background: We have previously shown that TIMI Myocardial Perfusion Grade (TMPG) 2 is associated with a two- fold increase in mortality rates in the setting of Acute MI in comparison with TMPG 3 (4.4%, 2.0%, respectively). The goal of this study was to objectively characterize the kinetics of myocardial perfusion in TMPG 2 vs TMPG 3. **Methods:** We hypothesized that dye inflow into the microvasculature is slower in TMPG 2 in comparison with TMPG 3. Data were drawn from 116 acute MI patients in the LIMIT AMI trial of tPA + rhuMAb CD18 (a WBC antibody) vs tPA + placebo. These 116 patients were assessed to have either a TMPG 2 (persistent dye stain at end of injection that fades by next injection) or a TMPG 3 (normal blush). The number of frames required for dye to 1st enter the myocardium & for dye to reach peak intensity in the myocardium were counted and converted to 30 frames per second. **Results:** There was no significant difference in the time for dye to first enter the myocardium; however the peak intensity of TMPG 2 occurred 41.6 frames or 1.5 seconds later. This delay held true when corrected for the Corected TIMI Frame Count(p=<0.001). **Conclusion:** While the time to initial appearance of dye in the microvasculature does not differ between TMPG 2 and 3, the time to peak intensity is delayed in the TMPG 2. The delay in peak intensity may be secondary to distal mirco-embolization, vasospasm or damage in the microvasculature. This may explain in part the poor outcomes among patients with TMPG's of 2.

	TMPG 2	TMPG 3	p-value
Frame Blush 1st Appears	49.3 ± 22.7 n=18	51.4 ± 23.4 n=95	NS
Frame of Peak Intensity of Blush	161.3 ± 36.44 n=18	119.7 ± 44.5 n=97	0.003
Diastole Blush 1st Appears	2.31 ± 1.15 n=18	2.27 ± 0.93 n=96	NS
Diastole of Peak Intensity	6.97 ± 2.01 n=18	5.21 ± 1.61 n=98	0.0001

1121-97 Frequency and Clinical Significance of Angiographic Evidence of Distal Embolization During Primary Angioplasty for Acute Myocardial Infarction

Felix Zijlstra, Jan Paul Ottervanger, Menko Jan de Boer, Henk Eenhuizen, Dirk Dijkstra, Jan C. A. Hoorntje, Harry Suryapranata, Arnoud W. J. van 't Hof. *Isala klinieken, hospital De Weezenlanden, Zwolle, The Netherlands*

Background: Although recognized as an important feature of atherosclerotic coronary disease, little is known about the frequency and prognostic importance of distal embolization during primary angioplasty for acute myocardial infarction. **Methods:** As part of a randomized trial of thrombolysis versus primary angioplasty, 194 patients with acute myocardial infarction were treated with primary angioplasty. None of the patients was treated with IIb/IIIa inhibitors or thrombolytics. Clinical information was collected for a mean of 5 years. Embolization was defined as a distal filling defect with an abrupt 'cutoff' in 1 of the periferal coronary artery branches of the infarct-related vessel, distal to the site of angioplasty. Enzymatic infarct size was estimated from cumulative release of lactate dehydrogenase (LDH Q72). **Results:** Distal embolization was present in 27 patients (14%). Mean age and gender were not different between the two groups. Patients with distal embolization had a larger enzymatic infarct size (mean LDH Q72 1612 vs 847, p < 005) and a lower ieft ventricle ejection fraction at discharge (42% vs. 51%, p < 0.01). Long-term mortality was significantly higher in patients with distal embolization (44% vs. 9%, p < 0.001). **Conclusions:** Distal embolization during primary angioplasty can be seen on the coronary angiogram in 14% of patients. It is a predictor of a large myocardial infarction and a worse prognosis. Additional pharmacologic interventions and/or mechanical devices should be studied to prevent distal embolization.

1121-98 Use of a Protection Device Offsets the Delay in Reperfusion on the Recovery of Angiographic Parameters in Primary PTCA

Gabor Sutsch, F. Wolfgang Amann, Sabina Murphy, C. Michael Gibson. *Cardiology, University Hospital Zurich, Zurich, Switzerland, UCSF, San Francisco, CA*

Background: There is evidence that prolonged symptom-onset-to-balloon time (SBT) for primary PTCA is associated with an increased mortality and lower rates of TIMI flow grade (TFG) 3, in particular with stenting. Possibly, stenting further aggravates the burden of ongoing myocardial ischemia by causing additional downstream embolization. **Methods:** In 34 patients (mean age 56±11) with acute MI (SBT < 12 hours, h) PTCA with stenting of the occluded infarct-related artery was performed in combination with the PercuSurge® distal protection device. Patients were divided according an arbitrary cut-off of 4 hours in two groups with fast (SBT < 4 h, n=12, group 1) or delayed (SBT > 4 h, n=22, group 2) PTCA. Groups were comparable with respect to gender, age, hemodynamics, pattern of the infarcted vessel (LAD: 25% and 36%, respectively), ejection fraction, and use of glycoprotein 2b/3a inhibition (75% and 64%, respectively). An angiographic core analysis assessed pre-post TFG, corrected TIMI Frame Counts (CTFCs) and tissue level perfusion (TIMI Myocardial Perfusion Grade; TMPG) **Results:**

	Group 1	Group 2	p<
SBT in min (range)	193±50 (85-240)	472±157 (250-740)	0.0001
TFG pre / post	0.17±0.4 / 2.96±1.4	0.18±0.4 / 2.98±0.1	n.s./n.s
CTFC pre / post	100 / 25.3±10.8	100 / 22.3±8.2	n.s./n.s
TMPG pre / post	0.6±0.9 / 2.0±1.1	0.7±1.1 / 2.0±1.2	n.s./n.s

(mean ± SD; p for unpaired comparison between the groups)

Conclusions: In this pilot study, the recovery of epicardial and myocardial perfusion is equally improved in fast and delayed reperfusion using distal embolization protection in PCI with stenting for acute MI. Clinical benefit and survival advantage need to be determined in adequately designed trials.

1121-99 Validation of Myocardial Perfusion Grades Using Digital Subtraction Angiography (DSA)

C. Michael Gibson, Lily L. Luu, Sarah R. Kermgard, Colin A. Hynes, Matthew H. C. Otten, Jessica S. Lim, Mark Appleby, Andrew Michaels, Susan J. Marble, Sabina A. Murphy, Hal V. Barron. *University of California San Francisco, San Francisco, CA*

Background: Previously we demonstrated that a semiquantitative visual scheme of grading tissue level perfusion (Myocardial Perfusion Grade, MPG) is related to mortality in AMI. We hypothesized that the different MPGs (MPG 0=little or no blush;MPG 1=stain that persists on next injection;MPG 2=stain that fades by next injection; MPG 3 = normal blush) would be related to tissue level perfusion when analyzed quantitatively using digital subtraction angiography (DSA). **Methods:** Data were drawn from 161 consecutive pts in the LIMIT AMI trial of tPA + rhuMAb CD18 (a WBC antibody) vs tPA + placebo & 88 normals (no AMI). The MPG & DSA were assessed 90 min. after lytic administration. DSA was performed at end diastole by aligning images before dye filled the myocardium with those at the peak of dye filling the myocardium to subtract spine, ribs, diaphragm & artery. **Conclusions:** Overall, AMI is associated with less myocardial perfusion on DSA (p<0.0001 for all), increased peak Gray (brightness), decreased rate of rise in Gray/sec, increased blush circumference, & lower rate of growth of circumference (cm/sec). However, these data validate quantitatively that in AMI, myocardial perfusion for MPG 3 (normal blush related to lower mortality) is similar to that in normal pts, & is associated with increased tissue level perfusion on DSA compared to MPG 0. While entry appears normal for MPG 1 & 2, dye exit from the myocardium is delayed.

MPG*	n	DSA Peak Gray	Growth in Gray / sec	Circumference (cm)	Circumference Growth (cm) / sec
0 in AMI	71	2.5 ± 4.9	0.75 ± 1.6	7.2 ± 7.9	2.2 ± 2.4
1 in AMI	19	13.0 ± 12.8	3.8 ± 4.4	17.8 ± 7.0	5.4 ± 4.2
2 in AMI	11	19.9 ± 10.8	4.0 ± 1.9	19.0 ± 11.8	4.2 ± 3.1

3 in AMI	60	10.3 ± 6.0	2.9 ± 1.9	18.8 ± 10.4	5.0 ± 2.4
All AMI	187	7.8± 8.9	2.1 ± 2.5	13.6 ± 10.7	3.7 ± 2.0
No AMI	88	10.9 ± 5.7	2.8 ± 1.4	19.4 ± 5.4	5.2 ± 2.0

*4 way of MPGs p<=0.0001 by Kruskal Wallis test of medians for all variables

1121-100 **Effects of Early ACE-Inhibition in Nonthrombolyzed Diabetic Patients With Acute Myocardial Infarction**

Claudio Borghi, Stefano Bacchelli, Daniela Degli Esposti, Eugenio Cosentino, Ettore Ambrosioni. *Department of Medicine-University of Bologna, Bologna, Italy*

Background. ACE-inhibitors (ACEI) have been demonstrated to be largely effective for the treatment of patients with either diabetes and coronary artery disease. **Methods.**The present study was carried out as a post-hoc analysis of the SMILE trial to evaluate the influence of diabetes on the efficacy of 6-week treatment with the ACEI zofenopril given early (< 24 hours from symptoms) in 1514 patients with non thrmbolyzed acute anterior myocardial infarction (AMI). The main oucome measures were 6-week combined occurrence of death and severe refractory CHF, as well as 1 year mortality rate. **Results.** The diabetic population (D+, n.183) was significantly older and showed a greater proportion of females and hypertensive subjects than non diabetics (D-,n.1331). These variables have bee used as co-variates to adjiust statistical analysis. After 6 weeks of the double-blind treatment a greater proportion of the D+ patients reached the primary end-point (18.3% vs 9.6%, 2p=0.001). The effects of zofenopril over the primary end-point were significantly enhanced in D+ (absolute red.: -9.7% vs -2.1, 2p=0.001). Cumulative mortality was greatly reduced in D+ (absolute red.-3.0% vs -1.5% 2p=0.01) as did early mortality (<24 hours) (absolute red.-6.1% vs -0.7%, 2p=0.013). The incidence of S-CHF was increased in D+ where we observed a greater reduction in absolute event rate after ACEI when compared to D- (-7.3% vs -0.9%, 2p=0.001). 1-year mortality was increased in D+ (15.2 % vs 11.4%). Surprisingly, the survival rate after 1 year was greatly improved by ACEI in D- (13.8 vs 9.1%, 2p=0.001) than in D+ (16.5% vs 13.7%, 2p=0.03) and these findings have been confirmed by the Kaplan-Meier approach. **Conclusions.** The results of the present study confirm the pivotal role of ACEI for the teratment of patients with diabetes. They also suggest that the benefit of ACEI in patients with diabetes is strictly related to active drug treatment that should be maintained irrespectively of post-MI LV function.

ORAL CONTRIBUTIONS

831 New Management Concepts of Acute Coronary Syndromes

Monday, March 19, 2001, 2:00 p.m.-3:30 p.m.
Orange County Convention Center, Room 230D

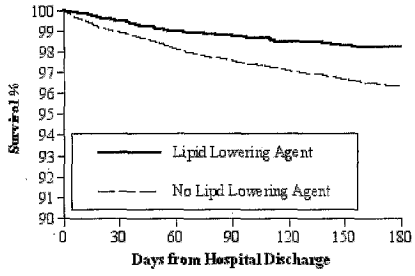
2:00 p.m.

831-1 **Stunning Reduction in Death and Myocardial Infarction Observed With Early Lipid Lowering Therapy After Acute Coronary Syndromes**

Herbert D. Aronow, Penny L. Houghtaling, Katherine E. Wolski, Eric J. Topol, Michael S. Lauer. *Cleveland Clinic Foundation, Cleveland, OH*

Background: Whether lipid lowering agents (LLA) reduce death or myocardial infarction (MI) when administered soon after an acute coronary syndrome (ACS) is unclear.
Methods: We compared the incidence of death and MI after an admission for ST elevation MI, non-ST elevation MI or unstable angina among patients from the GUSTO IIb and PURSUIT trials who were (n=3,653) or were not (n=17,156) discharged on LLA. A propensity analysis was used to match patients on the probability of receiving LLA at discharge. The resulting propensity score was entered into Cox models.
Results: Overall, there were 668 deaths. Treatment with LLA was associated with a marked mortality reduction by 30 days that was even greater at 6 months [Figure]. After adjusting for hyperlipidemia, other cardiac risk factors, type of ACS on presentation, discharge medications and other potential confounders, treatment with LLA was associated with a marked reduction in the incidence of death (Risk Ratio = 0.67, 95% CI 0.48-0.95), p = 0.023) and the composite death or MI (Risk Ratio = 0.80, 95% CI 0.66-0.99), p = 0.036) at 6 months.

Conclusion: In the largest international cohort study of this type to date, early lipid lowering therapy was associated with reduced death and MI after all types of ACS. Early initiation of LLA should be considered in all patients after an ACS.

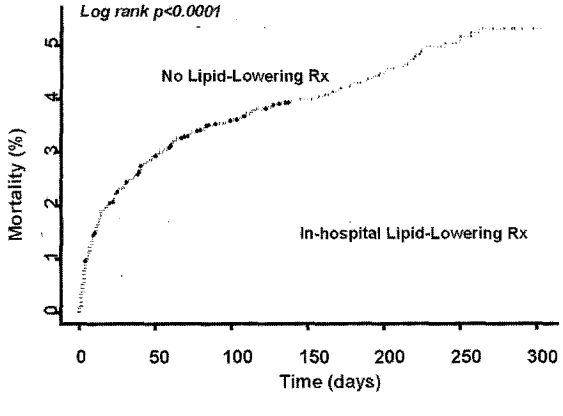


2:15 p.m.

831-2 **Early Statin Therapy Is Associated With Markedly Lower Mortality in Patients With Acute Coronary Syndromes: Observations From OPUS-TIMI 16**

Christopher P. Cannon, Carolyn H. McCabe, Jane Bentley, Eugene Braunwald. *Brigham and Women's Hospital, Boston, MA*

While statin therapy reduces mortality in patients with prior MI, few data are available on their early effects in patients with acute coronary syndromes (ACS). **Methods:** In the OPUS-TIMI 16 trial, patients with ACS (ranging from ST elevation MI to high-risk unstable angina) were treated with aspirin and randomized within 72 hours of symptom onset to the oral IIb/IIIa inhibitor orbofiban or placebo. In-hospital use of lipid-lowering therapies was assessed and mortality rates compared, with multiple Cox regression to adjust for baseline characteristics. **Results:** In 10,288 patients, lipid-lowering therapy was prescribed during hospitalization in 3883 (38%) of patients: 94% received statins, 7% received fibrates (with or without statins), <1% received niacin or resins. By 10 months, 90% of remained on lipid-lowering therapy and 34% had newly started therapy (97% statins). Treated patients were younger (age 59 vs. 61 years for non-treated, p<0.0001), but more often had prior MI (32% vs. 24%), Prior CABG 15% vs. 8%, or prior angina (30% vs. 25%)and more frequently received prior aspirin, beta-blocker, and other medical treatments, each p<0.0001. Mortality was significantly lower in patients treated with lipid lowering therapy: at 30 days 0.7% vs. 2.4% (p<0.0001). No differences in mortality were observed by which statin agent was used. The mortality difference persisted at 10 months 3.1% vs. 5.3% (p<0.0001).(Figure) Adjusted relative risks of mortality were 0.31 and 0.50 respectively each p<0.0001. This benefit was present in both placebo- and orbofiban-treated patients. **Conclusion:** In patients with acute coronary syndromes, we observed an significantly lower mortality that emerged early in the course of treatment among patients treated with statin therapy. If confirmed in randomized trials, these results provide further evidence of the benefit of early initiation of statin therapy in ACS.



2:30 p.m.

831-3 **Effects of Acute Hormone Therapy on Recurrent Ischemia in Postmenopausal Women With Unstable Angina**

Steven P. Schulman, David R. Thiemann, Pamela Ouyang, Nisha C. Chandra, Douglas S. Schulman, Steven E. Reis, Michael Terrin, Susan N. Townsend, Sandra Forman, Gary Gerstenblith. *Johns Hopkins Medical Institutions, Baltimore, MD, Maryland Medical Research Institute, Baltimore, MD*

Background: Endothelial vasodilator dysfunction occurs in atherosclerotic coronary artery disease and may contribute to the pathophysiology of unstable angina. Acute estrogen administration improves endothelial function in postmenopausal women with stable coronary artery disease. We conducted a randomized, double blind placebo controlled trial to determine whether acute hormone therapy reduces the incidence of ambulatory electrocardiographic (AECG) ischemic events over 48 hours in postmenopausal women with unstable angina. **Methods:** 293 patients were randomized to receive intrave-

nous followed by oral conjugated estrogen (E) plus medroxyprogesterone (MPA) for 21 days, intravenous followed by oral E for 21 days, or placebo (PLBO). The primary endpoint was the number of AECG ischemic events over the first 48 hours compared by t-tests.Clinical events were also determined over 6 months of follow-up. **Results:** The subjects were well matched in clinical characteristics and standard anti-ischemic medications were used. The AECG and clinical outcomes are shown below, all nonsignificant. The duration of AECG ischemia was also not different. 6-month events, including death, myocardial infarction, hospitalizations for recurrent angina, or need for revascularization also did not differ significantly among the 3 groups. **Conclusion:** Acute hormone therapy, when added to standard anti-ischemic therapy, does not reduce the number or duration of ischemic events, or the proportion of patients experiencing such events in postmenopausal women with unstable angina. This study adds to the growing evidence that hormone therapy may not benefit postmenopausal women with known coronary artery disease.

	E+MPA	E+PLBO	PLBO
Mean #AECG ischemic events/48 hrs	0.86	0.74	0.74
% of patients with AECG ischemia	14.1%	9.8%	10.9%
In-hospital symptomatic ischemia	52.1%	39%	42.4%
In-hospital myocardial infarction	3.2%	3.0%	5.1%
In-hospital death	5.3%	5.0%	3.0%

2:45 p.m.

831-4 **Low-Dose Urokinase and Enoxaparin Reduces the Incidence of Acute Myocardial Infarction in Patients With Unstable Angina or Non-qwave Myocardial Infarction**

Ji-Lin Chen, Collaborative Research Group of National Project Beijing China. *Cardiovascular Institute & Fu Wai Hospital, Beijing, People's Republic of China*

Background: Previous studies have shown increased rates of acute myocardial infarction (AMI) when high-doses of thrombolytic agents are used in the treatment of unstable angina. However, low-dose urokinase (UK) has been shown to be an effective anti-ischemic and anti-anginal therapy for patients with refractory angina pectoris, in combination with unfractionated heparin and aspirin. The aim of this study is to assess if the addition of low-dose UK to enoxaparin and aspirin therapy provides added benefits.
Methods: This study was a multicenter, single-blind, placebo-controlled, randomized clinical trial, conducted in 40 hospitals in China. Entry criteria were effort angina significantly aggravated within 5 days and angina at rest within 24 hours. 791 patients with unstable angina or non-Q wave myocardial infarction received either placebo or 5000IU/kg UK administered for 3 consecutive days. All patients also received aspirin 300 mg and enoxaparin 30 mg intravenous bolus plus 1mg/kg subcutaneous given in the hour before low-dose UK thrombolytic or placebo therapy on the first day of therapy; and subcutaneous enoxaparin 1 mg/kg q12 hours for 6 days and aspirin 300 mg/day for 6 days, then 100 mg/day (administered prior to UK on the second and third days of therapy). The primary endpoint for the comparison between the low-dose UK and placebo groups was death and AMI (cardiac event) within 30 days of enrollment.
Results: Although the combined endpoint of death and AMI was not significantly reduced in the low-dose UK group (2.0% vs. 4.0% placebo group, p = 0.147) the rate of AMI (0.05% vs. 2.5% placebo group, p=0.037) and the number of patients with frequent recurrent angina (first week results; 29.3% vs. 41.1% placebo group, p=0.001; fourth week results; 5.9% vs. 11.2% placebo group p=0.01) was significantly lower.
Conclusions: The addition of low-dose UK to a regimen of enoxaparin and aspirin appears to reduce the frequency of AMI and recurrent angina in patients with unstable angina/non-Q-wave myocardial infarction remarkably.

3:00 p.m.

831-5 **The Effects of Beta Blocker Therapy in Patients With Acute Coronary Syndromes Undergoing Percutaneous Intervention: EPIC, CAPTURE, and RAPPORT Data Bases**

Byron K. Ellis, A. M. Lincoff, Shelly Sapp. *Cleveland Clinic Foundation, Cleveland, OH*

Background: Various clinical trials have shown the beneficial effects of beta blockers in patients with coronary artery disease and congestive heart failure. This study evaluates the effects of beta blockers in patients undergoing percutaneous intervention (PCI) in the setting of unstable angina or myocardial infarction (MI).
Methods: Using data bases from the EPIC, CAPTURE and RAPPORT randomized placebo-controlled trials, a total of 2,163 patients were studied. Only a subset of patients were studied from the EPIC trial, consisting of those patients presenting with unstable angina or acute MI. These trials evaluated the glycoprotein IIb/IIIa inhibitor, abciximab, during coronary intervention. Beta blockers were administered to 1405 patients either prior to or at the time of enrollment, and 758 patients did not receive beta blocker therapy. The end points were death, MI and urgent revascularization at 30 days and 6 months.
Results: Death was significantly reduced at 30 days and 6 months in patients receiving beta blocker therapy.

End Points	Follow Up	No Beta Blocker	Beta Blocker	p-value
Death	30 days	16 / 758(2.1)	12 / 1405(0.9)	0.013
	6 months	31 / 758(4.2)	30 / 1405(2.2)	0.009
MI	30 days	30 / 758(4.0)	49 / 1405(3.5)	0.554
	6 months	44 / 758(5.9)	86 / 1405(6.2)	0.832
Revasc.	30 days	27 / 758(3.6)	61 / 1405(4.4)	0.411
	6 months	154 / 758(21.2)	344 / 1405(25.1)	0.048

Conclusion: The use of beta blockers in patients undergoing PCI with acute coronary syndromes is associated with a statistically significant reduction in short term mortality.

3:15 p.m.

831-6 **Is Initial Treatment With Enoxaparin Beneficial in Unstable Angina/Non-ST Segment Elevation Patients Who Later Undergo Percutaneous Coronary Intervention (PCI)?**

Keith A. A. Fox, Elliott M. Antman, Marc Cohen, Frederique Bigonzi, David Radley, On behalf of the ESSENCE & TIMI 11B investigators. *The Royal Infirmary of Edinburgh, Edinburgh, United Kingdom*

Background. Combined analysis of ESSENCE and TIMI 11B demonstrated that enoxaparin is superior to unfractionated heparin (UFH) in patients with unstable angina (UA)/non-ST-segment elevation myocardial infarction (MI): 7.1% vs 8.6% (p=0.02) death/MI at 43 days. Decisions to proceed to revascularization were independent of trial randomization.
Methods We analyzed a population comprising 6098 patients for death or MI at 43 days using chi-squared tests; 983 patients undergoing coronary artery bypass grafting were excluded. Clinicians were blinded to enoxaparin vs UFH (unfractionated heparin).
Results PCI was not randomized but was performed at the discretion of the treating physician. Results are shown in Table 1.
Conclusion Patients undergoing PCI (compared with those who were not) sustained more events, including events prior to PCI, consistent with a higher risk population. Enoxaparin treatment, when compared with UFH treatment, benefited both patients treated solely medically, and those patients who underwent PCI following an initial period of medical stabilization.
Table 1.

Patients undergoing PCI within 12 hrs of final dose:	UFH n / N (%)	Enoxaparin n / N (%)	RR (+/-95CI)
Patients with PCI:			
Death/MI post-PCI	14 / 237 (5.9%)	7 / 198 (3.5%)	0.60 (0.25, 1.45)
All Death/MI	25 / 237 (10.5%)	20 / 198 (10.1%)	0.96 (0.55, 1.67)
Patients without PCI:			
All Death/MI	196 / 2783 (7.0%)	167 / 2880 (5.8%)	0.82 (0.67,1.01)
All patients undergoing PCI during hospitalization:	UFH n / N (%)	Enoxaparin n / N (%)	RR (+/-95CI)
Patients with PCI:			
Death/MI post-PCI	34 / 482 (7.1%)	18 / 424 (4.3%)	0.60 (0.34,1.05)
All Death/MI	56 / 482 (11.6%)	43 / 424 (10.1%)	0.87 (0.60,1.27)
Patients without PCI:			
All Death/MI	165 / 2538 (6.5%)	144 / 2654 (5.4%)	0.83 (0.67,1.04)

POSTER SESSION

1150 Treatment Strategies for Cardiac Ischemic Syndromes

Monday, March 19, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 4:00 p.m.-5:00 p.m.

1150-79 **TIMI Risk Score to Predict 6-Month Mortality, Recurrent Cardiac Events, and Relative Benefit of Invasive vs. Conservative Strategy in Patients With Unstable Angina: Results From TACTICS-TIMI 18**

Christopher P. Cannon, William S. Weintraub, Laura Demopoulos, Peter DiBattiste, Debbie Robertson, Paul deLucca, Carolyn H. McCabe, Elliott M. Antman, Eugene Braunwald, for the TACTICS-TIMI 18 Investigators. *Brigham and Women's Hospital, Boston, MA*

The Thrombolysis In Myocardial Infarction (TIMI) Risk Score for acute coronary syndromes has been shown in several studies to predict both prognosis and response to new therapies such as low-molecular weight heparin or glycoprotein IIb/IIIa inhibitors. We sought to validate the TIMI Risk Score and assess its usefulness in predicting benefit of an invasive vs. conservative strategy. **Methods:** In the TACTICS-TIMI 18 trial patients with unstable angina or non-ST elevation MI were treated with aspirin, heparin and tirofiban and randomized to an invasive strategy with routine catheterization and revascularization as appropriate within 4-48 hours, or to a conservative (i.e., a "selective invasive" strategy) with catheterization performed only if the patient had objective evidence of recurrent ischemia or a positive stress test. We used the TIMI risk score by calculating the number of the 7 predictor variables each patient had: age >65 years, at least 3 risk factors for coronary artery disease, prior coronary stenosis of >=50%, ST deviation on ECG, severe angina, prior aspirin, and elevated cardiac markers. We then compared mortality and outcomes across the TIMI risk scores. **Results:** Preliminary results as of 8/2000 showed among the 2220 patients, there was a gradient in 6-month mortality for

increasing TIMI Risk Score.(See Table) Similarly, the primary (composite) endpoint of death, MI or rehospitalization for acute coronary syndrome was significantly higher as TIMI Risk Score increased.

TIMI Risk Score	0/1	2	3	4	5	6/7	P trend
N=	161	450	735	576	239	59	
Mortality (%)	1.9	1.6	2.0	5.2	4.6	11.9	<0.001
Composite (%)	7.45	13.8	16.2	19.4	22.6	32.2	<0.001

Conclusion: The TIMI Risk Score was a significant predictor of 6 month mortality, and recurrent cardiac events. Its use in predicting benefit of a routine invasive vs. "selective invasive" strategies will be presented.

1150-80 Percutaneous Coronary Intervention Versus Coronary Bypass Graft Surgery: Outcome of Diabetics in the AWESOME Randomized Trial and Registry

Steven P. Sedlis, Douglass A Morrison, Gulshan Sethi, Jerome Sacks, William Henderson, Frederick Grover, Rick A. Esposito, for the Investigators and Patients of VA cooperative #385 (AWESOME). *New York VA Medical Center, New York, NY*

Background: Prior studies indicate that coronary bypass graft surgery may be superior to percutaneous coronary intervention for diabetics, but coronary bypass graft surgery has not been previously compared to percutaneous coronary intervention for diabetics at high risk for surgery. This study compares the three year survival of diabetics with coronary bypass graft surgery versus percutaneous coronary intervention in a randomized trial and registry of such high risk patients. **Methods:** AWESOME was a five-year (1995-2000), sixteen site, Veterans Affairs, prospective, randomized trial and registry experience comparing coronary bypass graft surgery to percutaneous coronary intervention in patients with medically refractory unstable angina and one or more high-risk factors (prior heart surgery; myocardial infarction within 7 days; left ventricular ejection fraction<.35; age>70 years; intra-aortic balloon required to stabilize). percutaneous coronary intervention could include both stents and glycoprotein IIb/IIIa receptor blocking drugs and bypass surgery could include off-pump or innovative myocardial protection. Of the 454 patients in the AWESOME randomized trial, 144 (32%) had diabetes; of the 327 in the patient refused registry, 89 (27%) had diabetes; and of the 1650 patients in the physician assignment registry, 525 (32%) had diabetes. **Results:**

	6 month		36 month		log-rank
diabetic	CABG	PCI	CABG	PCI	
Random	86%	91%	73%	80%	p=0.40
Patient refused	85%	97%	85%	91%	p=0.0.35
Physician assignment	87%	86%	72%	73%	p=0.40
non-diabetic	CABG	PCI	CABG	PCI	
Random	92%	96%	80%	79%	p=0.80
Patient refused	92%	96%	81%	88%	p=0.30
Physician assignment	90%	91%	78%	79%	p=0.40

Conclusions: We conclude that percutaneous coronary intervention is a relatively safe alternative to bypass surgery for diabetic patients with medically refractory unstable angina who are at high risk for coronary bypass graft surgery. Patients and physicians are able to choose between these two very different revascularization options for these patients.

1150-81 Comprehensive Analysis of Death and Nonfatal Myocardial Infarction During the First Twelve Months Following Acute Nonq-Wave Myocardial Infarction: Comparison of Invasive Versus Conservative Strategies in the VA Non Q-Wave Infarction Strategies In-Hospital (VANQWISH) Trial

Arun K. Kolli, Michael J. Wade, Robert A. O'Rourke, Alvin S. Blaustein, William E. Boden. *Veterans Affairs Medical Center, Syracuse, NY, Hartford Hospital, Hartford, CT*

Background: The overall results of the VANQWISH Trial indicate that long-term (mean: 23 months; range: 12-44 months) clinical outcomes for the composite primary end point (death or non-fatal [NF] myocardial infarction [MI]) were similar in patients (pts) randomized to an early ischemia-guided (IG) strategy compared to a "routine invasive" (R-INV) strategy. However, in the first 12 months, pts randomized to the R-INV strategy had significantly worse outcomes than those in the IG strategy, with a significantly higher rate of combined events (death or MI) and death alone. In order to better elucidate these findings, we performed a comprehensive analysis of all deaths and MIs that occurred in pts randomized to the two management strategies during the first post-MI year. **Methods:** 920 pts were randomized to either an IG strategy (n=458) or a R-INV strategy (n=462). The IG strategy group was further divided into 2 groups: a) pts who remained without coronary angiography during 12 months of follow-up ("conservative arm"[CON], n=236), and; b) pts with inducible ischemia who met pre-defined criteria for coronary angiography followed by revascularization if coronary anatomy was feasible ("selective invasive" arm [S-INV], n=222). **Results:** Multivariate analyses revealed that the R-INV arm had worse 12-month outcomes than the CON arm (hazard ratio [HR]=2.2; P<0.001 for combined events; HR=1.8; P=0.04 for death alone; HR=2.2; P=0.01 for NFMI alone). Compared to the CON arm, pts in the S-INV arm had significantly more composite events (HR=2.3; P<0.001) and NFMI (HR=3.2; P<0.001), but no difference in 1-year survival (HR=1.2; P=0.52). When clinical outcomes between the S-INV and R-INV arms were compared, there was no difference in composite events (HR=1.1; P=0.6), mortality (HR=0.7; P=0.21) or NFMI (HR=1.5; P=0.052). **Conclusion:** Better outcomes at 12 months were achieved in the early IG strategy in VANQWISH, particularly those in the CON subset who remained low-risk. An initial "ischemia-guided" approach to the management of NQMI permits appropriate risk stratification of patients into distinct subsets resulting in improved 1-year clinical outcomes that can be tailored to the level of risk.

1150-82 The Effect of Clopidogrel vs Aspirin on Recurrent Clinical Events and Total Vascular Mortality: Results From the CAPRIE Study

James J. Ferguson, Rollo P. Villareal, Edward K. Massin. *Texas Heart Institute, Houston, TX*

Background: The CAPRIE study compared the thienopyridine clopidogrel with aspirin in patients with atherothrombotic disease; the primary outcome cluster was a composite of new first events. However, since recurrent events are also a significant contributor to subsequent overall clinical outcomes, we analyzed total events (initial and recurrent) and total vascular mortality (fatal MI, fatal stroke, and other vascular death) in CAPRIE.
Methods: A retrospective analysis of the CAPRIE patient cohort (n=19,185), including both initial events (fatal/non-fatal MI, fatal/non-fatal stroke, other vascular death) and subsequent vascular events.
Results:

	Aspirin (n=9586)	Clopidogrel (n=9599)	% Decrease
Initial Events	1021	939	8.2 % *
[* primary outcome cluster: 8.7% RRR by Cox Proportional Hazard Model]			
Subsequent Events			
MI	43	33	23.4 %
Stroke	84	71	15.6 %
Other vascular death	35	34	3.0 %
Total	303	256	15.6 %
TOTAL Events	1324	1195	9.9 %
Initial vascular death	321	308	4.2 %
Recurrent vascular death	57	42	26.4 %
Total vascular death	378	350	7.4 %

The net reduction in total events (both initial and recurrent) with clopidogrel was 14 events/1000 patients; the net reduction in total vascular death (both initial and recurrent) was 3/1000.
Conclusions: In CAPRIE, clopidogrel was significantly superior to aspirin in preventing both initial and subsequent vascular events. The total events prevented (14/1000 patients) and total vascular deaths prevented (3/1000) may be more representative of the potential clinical benefits of clopidogrel over aspirin.

1150-83 Safety of Abciximab in Addition to the Lmw Heparin Dalteparin as the Primary Treatment of Acute Coronary Syndromes (ACS)

S James, M Pfisterer, S Husted, F Kontny, M Nieminen, L Wallentin. *Department of Cardiology, Uppsala, Sweden*

The combination of aspirin and lmw heparin is at present the routine initial treatment of acute coronary syndromes in many patients. So far the safety and efficacy of the addition af abciximab to lmw heparin as the primary medical treatment in acute coronary syndrome (ACS) has not been evaluated. **Methods:** As a substudy within the multi-national multicenter prospective double-blind trial of the efficacy of abciximab as the primary medical treatment in ACS without early revascularization 974 of the 7800 patients used subcutaneous treatment with dalteparin 120 IU/Kg b.w. (max. dose 10.000 IU)for 5 – 7 days instead of the routine 48 hours heparin infusion. The patients were randomized to bolus injection followed by 24 hours (n=315) or 48 hour (n=331) infusion of abciximab or corresponding placebo (n=328). The primary endpoint was safety at 30 days follow up. As in the main trial there were no significant differences in efficacy by the addition of abciximab.

Results	Dalteparin n=328	Heparin n=646	Results n=2270	Dalteparin n=4556
Any stroke	1.2%	1.1%	0.6%	0.6%
Intracranial haemorrhage	0	0.31%(2)	0.1%(2)	0.15%(7)
Ischemic stroke	1.2%(4)	0.8%(5)	0.4%(9)	0.44%(20)
Any Bleeding (non-CABG)				
Major (TIMI)	0.7%	1.3%	0.2%	0.8%**
Minor	1.3%	4.0%*	1.6%	3.2%***
Platelet count (<50K/mL)	0%	0.8%	0%	1.6%***

*p<0.05, **p<0.01, ***p<0.001
Conclusion: Combination of abciximab with full dose LMWH (dalteparin) seems as safe as its combination therapy with reduced dose standard heparin. In both cases there is a slight excess in bleeding with combination therapy.

POSTER SESSION

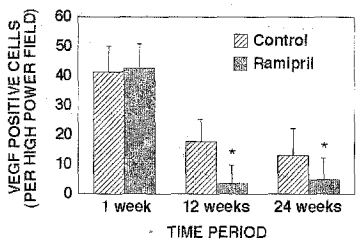
1151 Regulation of Angiogenesis and Coronary Flow in Myocardial Infarction

Monday, March 19, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 4:00 p.m.-5:00 p.m.

1151-84 Angiotensin Converting Enzyme Inhibitor Reduces VEGF Expression by Cardiac Myofibroblasts in Healing Infarct Scar Tissue and Attenuates Ventricular Remodeling

Samuel A. Wickline, Qingyan Zhu, Heather Lewis, Christopher Hall, John Allen, Michael Scott, Gregory Lanza. *Washington University, St. Louis, MO*

To define the time course of expression of VEGF in cardiac remodeling after infarction, the cell types involved, and the role of the renin-angiotensin system in VEGF regulation, myocardial infarction was induced by left coronary artery occlusion in 33 Sprague-Dawley rats. Ramipril (1 mg/kg/d) was administered in drinking water starting 3 days after infarction and continued for 1,12 or 24 weeks in 5, 8, and 5 infarct rats, and placebo was administered to 4, 7, and 4 infarct rats, respectively. VEGF was quantified by immunocytochemical analysis of the averaged number of positive cells in 8-10 contiguous high power fields. The Figure demonstrates prominent VEGF expression early after infarction, which declines thereafter ($p<0.05$ for time dependence, by ANCOVA to control for infarct size). Ramipril significantly reduced VEGF expression at later time periods ($p<0.05$ for treatment effects at 12 and 24 weeks). Ramipril also limited ventricular remodeling: relative heart mass decreased by 17% at 12 weeks and 20% at 24 weeks as compared with values for untreated rats ($p<0.05$ each). Imunocytochemical analysis of cells containing μ-smooth muscle actin (μ-SMA), a marker for myofibroblasts, indicated that the majority of cells expressing VEGF at all time periods were tissue myofibroblasts, which was confirmed by double immunostaining for VEGF and μ-SMA. We conclude that: 1) VEGF expression in healing infarct scars is time dependent and is regulated by the renin-angiotensin system; 2) myofibroblasts are the predominant cell types that express VEGF in chronic cardiac wound healing after infarction; and 3) ACE inhibitors coordinately reduce remodeling and scar tissue VEGF expression independent of infarct size. These data suggest that ACE inhibitors alter the natural history of scar tissue wound healing after infarction, including obligate angiogenic responses attributable to cell types such as the myofibroblast.



1151-85 Cardiomyoplasty and Treatment Improve Left Ventricular Function and Myocardial Revascularization After Myocardial Infarction in Rats

Katia L. D. De Angelis, Maria Cláudia Irigoyen, Adolfo A. Leiner, Idágene A. Cestari. *Biengineering Division, Heart Institute (Incor), Medical School, Federal University of São Paulo, São Paulo, Brazil*

Background: Myocardial infarction can cause complex architectural changes that have an important bearing on ventricular function. We tested the hypothesis that cardiomyoplasty (CDM) combined with VEGF treatment in the setting of experimentally induced myocardial infarction (MI) would stimulate angiogenesis and reduce the hemodynamic deficit. **Methods:** Male Wistar rats were divided in five experimental groups: intact (C, n=6), CDM (n=6), MI (left coronary artery ligation; n=5), CDM performed 14 days after MI (MI+CDM, n=6) and MI+CDM associated to VEGF treatment (MI+CDM+VEGF, n=5). Recombinant human VEGF165 was infused (25 mg) into the left latissimus dorsi (LD) main artery immediately before CDM. End-diastolic pressure (EDP) was obtained by left ventricle cannulation. Regional flows and cardiac output (CO) were measured by the injection of colored microspheres into the left ventricle (300.000, blue) at day 56. Collateral blood flow (CF) from LD to the myocardium (CF LD-M) was determined by the ratio of yellow microspheres (50.000 injected into the LD main artery) counted in myocardium to that counted in LD, whereas the CF from the myocardium to the LD (CF M-LD) was determined by the ratio of blue microspheres counted in LD to that counted in the myocardium. **Results:** The ratio of left ventricle to body weight (LV/BW) and end-diastolic pressure (EDP) were reduced after CDM in MI rats. No differences were found between groups in CO and coronary flow. VEGF treatment was associated with an increase in the CFLD-M in MI rats submitted to CDM. CF M-LD was greater in VEGF group compared to CDM and MI+CDM.

	C	CDM	MI	MI+CDM	MI+CDM +VEGF
LV/BW	2.5±0.05	2.8±0.08	3.4±0.12*#	2.9±0.08*+	3±0.14*+
EDP (mmHg)	-0.14±0.5	-0.44±1.2	15.35±3.3*#	4.77±1.8+	3.9±2+
CO (mLmin-1)	62.5±6.6	74±4.6	49.5±4.5	71.5±11.8	76±9.6
CFLD-M (%g-1)	0.89±0.89		4.41±1.45#	24.85±10#‡	
CFM-LD (%g-1)	5.49±2.35		3.88±2.34	9.5±2.6#‡	

*p<0.05 vs. C;#p<0.05 vs. CDM;+p<0.05 vs. MI;‡p<0.05vs.MI+CDM

Conclusion: Cardiomyoplasty improved left ventricle function after myocardial infarction. In this setting, VEGF treatment may offer an alternative route to myocardial revascularization.

1151-86 Effects of Angiotensin II Type 1 Receptor Blockade and Angiotensin Converting Enzyme Inhibitor on the Ventricular Remodeling After Myocardial infarction- With Special References to Sarcoplasmic Reticulum and Its mRNA

Eiichi Geshi, Takashi Katagiri. *Third Department of Internal Medicine, Showa University School of Medicine, Tokyo, Japan*

We clarified the role of renin-angiotensin system and its relation with ventricular remodeling after myocardial infarction with the influences of Ca-ATPase activity of the sarcoplasmic reticulum (SR) and its mRNA (SERCA2a) using angiotensin type 1 receptor blockade (AT1B) and angiotensin converting enzyme inhibitor (ACEI). **Material and method:** Myocardial infarction was induced by the ligation of the LAD in 40 SD rats. They were divided into 4 groups: 1) V group, vehicle treated; 2)AT1B group, Candesartan treated; 3)ACEI group, Captopril treated; and 4) C group, sham operated. After 4 weeks, hemodynamic measurements (HR, LVP and left ventricular end diastolic pressure (LVEDP)) and biochemical (Ca-ATPase activity of SR and SERCA2a) and histological analyses (transverse diameter of myocyte and % of interstitial fibrosis) of the non-ischemic portion were performed. **Result:** There were no significant changes in HR and LVPs between each group. While LVEDP was significantly higher in the V group than in the C group, it was maintained at low levels in both the ATIB and ACEI groups. Ca-ATPase activity of SR was significantly lower in the V group (3.06 micromoles Pi/mg protein/hr) than in the C group (5.82), but the values in the treated groups were significantly higher (ATIB; 5.10, ACEI; 5.04). In the northern blot analysis, the SERCA2a/beta-actin was significantly lower in the V group (1.88) compared to the C group (3.38), while values in ATIB (3.08) and ACEI (2.86) groups were higher. In the histological observations, hypertrophy of myocytes and interstitial fibrosis were observed more in the V group (transverse diameter, 8.16 micrometer, and interstitial fibrosis, 11.21%) than in the C group (7.03 and 9.69), and these changes were diminished similarly by treatments with ATIB (7.18 and 10.02) and ACEI (7.29 and 9.98). **Conclusion:** Treatments of AT1B and ACEI showed similar beneficial effects on the infarcted heart. We concluded that renin-angiotensin system acts as one of the key factors in the ventricular remodeling after myocardial infarction.

1151-87 Induction Of Transforming Growth Factor beta And Connective Tissue Growth Factor Expression During Myocardial Ischemia-Reperfusion Injury

Bysani Chandrasekar, Gary R. Grotendorst, Gregory L. Freeman. *University of Texas Health Science Center, San Antonio, TX, University of Miami School of Medicine, Miami, FL*

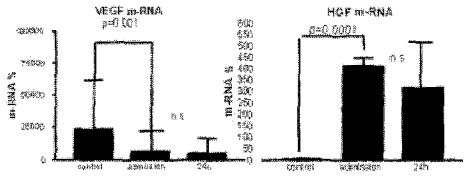
Background: The growth factors involved in post-infarct tissue healing and subsequent left ventricular remodeling are not fully known. Hence, the goal of the present study was to evaluate the expression and localization of transforming growth factor beta (TGF b) and connective tissue growth factor (CTGF) following myocardial ischemia-reperfusion injury. **Methods:** In 32 WKY rats, the LAD coronary artery was occluded for 45 min, and reperfused (R) for 15, 30 min, 1, 2, 3, and 6, 24 hours, and 7 days (n=4/group). Sham-operated animals served as controls (n=4). Following reperfusion, part of the tissue containing ischemic and adjacent non-ischemic tissue were embedded in OCT for immunohistochemistry (IHC). For mRNA and protein analyses the ischemic portion was separated from the non-ischemic zone, and was snap frozen. **Results:** Northern blot analysis revealed TGF b mRNA in controls. In reperfused animals, levels of TGF b fell at 1 h R, and increased significantly at 3 h R, and remained elevated until 7 days. Protein levels followed a similar pattern as that of mRNA. In contrast, CTGF mRNA was not detected in controls. It was detected in reperfused animals at 2 h, and remained elevated thereafter. However, CTGF protein was detected at 3 h, increased further at 6 h, and remained at these high levels until 7 days. IHC revealed intense but diffuse TGF b immunoreactivity throughout the myocardium in controls. In reperfused myocardium, intensity of TGF b immunoreactivity was much higher in the non-ischemic tissue at 6 and 24 h R. At 7 days, TGF b was detected in both ischemic and non-ischemic zones at similar levels. While CTGF immunoreactivity was not detected in controls or in reperfused myocardium until 2 h, weaker but diffuse staining was present in both the ischemic and non-ischemic zones. Its intensity increased by 3 h, and remained at these high levels until 7 days. **Conclusions:** Following ischemia-reperfusion, both TGF b and CTGF are expressed. However, TGF b is expressed earlier than CTGF, indicating that TGF b might have induced CTGF expression. Together, these growth factors may participate in the deposition of extracellular matrix and subsequent remodeling.

1151-88 Different Origin From Elevated Hepatocyte- and Vascular Endothelial Growth Factor Serum Levels in Patients After Myocardial Infarction. Role of Leukocyte Activation

Achim Gutersohn, Jr., Ahmet H. Elmaagacli, Thomas Budde, Jochen Buchholz, Ulrich W. Schäfer, Raimund Erbel. *University of Essen, Essen, Germany, ALfried Krupp Hospital, Essen*

Background: Leukocytes play an important role in inflammation yet it remains unclear how they interact during myocardial ischemia. Hepatocyte Growth Factor (HGF) and Vascular Endothelial Growth Factor (VEGF) are involved in angiogenesis, wound healing, tissue differentiation and vasorelaxation. They are both supposed to be cardioprotective. After acute myocardial infarction (AMI) serum HGF and VEGF levels are elevated

although the origin remains unknown. **Methods:** Blood was obtained from patients submitted to the hospital with diagnosis of AMI before any intervention and 24 hours after. 20 healthy volunteers were recruited consecutively. Concentrations of HGF and VEGF m-RNA transcripts in human leukocytes were measured quantitatively using the newly established real time polymerase chain reaction (PCR). **Results:** A 95 fold increase in HGF m-RNA concentration at admission (412.03%) and an additional increase after 24h compared to control group (4.32%) was measured. VEGF m-RNA concentrations in leukocytes were low at admission (1085.9%) and 24h after AMI compared to control group (23652.5%). **Conclusion:** Early increase of HGF after AMI is due to an upregulation of HGF m-RNA in leukocytes. Though HGF m-RNA concentrations remained elevated VEGF m-RNA decreased. Serum VEGF therefore may originate from myocardium itself. Both mitogens are important in post AMI repair regulation and reperfusion. Our results undermine that leukocytes take an active role in reperfusion and myocardial repair.



1151-89 Pharmacokinetics and Efficacy of Intravenous Vascular Endothelial Growth Factor (rhVEGF) in Porcine Hibernating Myocardium

Shankha S. Biswas, Patrick W. Domkowski, Luis H. Diodato, Anne M. Pippen, Kevin P. Landolfo, Brian H. Annex. *Duke University Medical Center, Durham, NC*

Background: In porcine hibernating myocardium, we have demonstrated changes in myocardial blood flow (MBF) and function with laser and angiogenic therapies. The purpose of this study was to examine the pharmacokinetics (PK) and long-term efficacy of intravenous (IV) rhVEGF (total 30 g/kg) in hibernating myocardium. **Methods:** Eight mini-swine with 90% left circumflex artery (LCX) stenosis and documented hibernating myocardium by positron emission tomography (PET) and dobutamine stress echocardiography (DSE) were randomized to IV rhVEGF (50 ng/kg/min for 200 minutes at 3 72 hour intervals, n=6) or IV vehicle (n=2). As an additional control, 6 pigs had 30 intramyocardial vehicle (IM) injections. PK parameters were calculated using non-compartmental analysis and compared to published human data. After 3 and 6 months, PET and DSE were repeated. DSE detects ischemia by changes in regional wall motion score index (WMSI) where 1 normal, 2 hypokinetic, 3 akinetic, and 4 dyskinetic. **Results:** The plasma clearance (14.8 mL/min/kg) was biphasic with a large volume of distribution (Vss 1530 mL/kg) and a terminal half-life of 71 minutes after IV rhVEGF. The rapid clearance and large Vss suggests extensive tissue binding and is similar to the PK parameters reported in humans (Cl 22 mL/min/kg; t1/2 77 min; Vss 1690ml/kg). With IM and IV vehicles, MBF did not increase significantly over baseline at 3 months (6.7±8.2% and 8.6±8.9%) or 6 months (6.9±6.7% and 0.54±0.59%). With rhVEGF, MBF increased by 4.7±3.8% over baseline at 3 months (p=0.25), and by 22.0±5.8% at 6 months (p=0.003). At 3 months, resting and peak stress LCX WMSI trended towards less ischemia with rhVEGF (2.1±0.20 and 1.6±0.20 vs 2.2±0.21 and 1.8±0.24 at baseline, p=0.10 for both). At 6 months, resting and peak stress WMSI demonstrated significant reduction in ischemia (1.9±0.25, p=0.02 and 1.5±0.18, p=0.04 vs baseline). No ischemic changes were seen with IM or IV vehicle. **Conclusions:** Using a dosing regimen yielding a similar PK profile to humans, IV rhVEGF significantly improved regional MBF, as well as resting and stress-induced ischemia in porcine hibernating myocardium.

1151-90 Characterisation of a Model of Chronic Coronary Artery Stenosis in the Rat by Cine-MRI

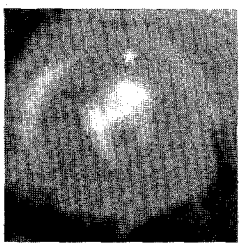
Matthias Nahrendorf, Karl-Heinz Hiller, Kai Hu, Christiane Waller, Axel Haase, Georg Ertl, Wolfgang R. Bauer. *Wuerzburg University, Wuerzburg, Germany*

Background: Chronic coronary artery stenosis is a disease with a high incidence. Aim of the study was to non-invasively characterize a model of chronic artery stenosis in the rat, which could be a research tool for the search of novel therapies of this condition. **Methods:** Stenosis was induced by a ligation including a 300µm wire placed next to the left coronary artery. The wire was taken away immediately after the suture was closed. MRI-scans were done 2 weeks after induction of stenosis in a 7 T-scanner using an ECG-triggered Cine-FLASH-sequence: 16 short axis slices, slice thickness 1 mm, echo-time 1.2 ms, resolution 200 µm. Left ventricular (LV) mass, LV volumes, cardiac output (CO), ejection fraction (EF), end-diastolic wall thickness of the area associated to the stenosis (ST) and a remote region (EDW) and systolic wall thickening of both regions (SWT) were determined in 7 wistar rats and compared to 11 controls. Occlusion of the coronary was excluded by 3D-MR-Angiography of the isolated perfused heart. **Results:** There was no difference in LV mass and heart rate between groups.

	control	stenosis
EDV (µl)	169.7+/-8.5	196.2+/-32.3
SV (µl)	124.7+/-6	83.2+/-9.1*
CI (ml/kg/min)	142.5+/-6	97.5+/-12,5*
EF %	74+/-2	44.3+/-3.0*
EDW (mm)	2.1+/-0.05	2.1+/-0.05/ ST: 1.6+/-0.1*
SWT (%)	62.5+/-4.1	54.3+/-5.4/ ST:18.6+/-10.3*

mean+/-SEM. *p<0.01 vs control.

Conclusion: Cine FLASH MRI proved to be a valuable tool for non-invasive characterisation of little known small animal models. Induction of coronary stenosis led to worsening function of the associated myocardial segment with consecutive impairment of global LV function. Regional SWT was improved by dobutamine stress but did not reach control values. This model of chronic ischemia is well suited for tests of novel therapies.



POSTER SESSION

1152 Stabile Ischemic Syndrome: Medical Therapies

Monday, March 19, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 4:00 p.m.-5:00 p.m.

1152-92 Comparative Antianginal Efficacy and Tolerability of Ranolazine in Diabetic and Nondiabetic Patients: Results of the MARISA Trial

Vincent DeQuattro, Sandra Skettino, Bernard R. Chaitman, Peter C. Hanley, Petr Jansky, J. K. Kuch, John O. Parker, J. J. Nelson, David Hebert, Andrew A. Wolff. *University of Southern California, Los Angeles, CA, CV Therapeutics, Palo Alto, CA*

Background: Ranolazine is a partial fatty acid oxidation (pFOX) inhibitor that shifts ATP production away from fatty acid oxidation toward more oxygen-efficient glucose oxidation. Because of the metabolic shift toward glucose oxidation, data from diabetic patients were examined. **Methods:** The MARISA (Monotherapy Assessment of Ranolazine In Stable Angina) study randomized patients to ranolazine 500 mg, 1000 mg and 1500 mg bid and placebo in a double-blind, 4-period crossover design study. All patients performed a modified Bruce exercise test at the time of trough and peak drug levels on each treatment; 42 patients with diabetes were compared to 133 non-diabetic patients. **Results:** Exericse duration (see table), time to angina and time to 1 mm ST segment depression were prolonged by ranolazine at the time of both peak and trough drug levels (treatment p-values <0.001) and generally increased with dose. At peak and trough, ranolazine effects were similar in diabetic and non-diabetic patients (treatment by diabetes interaction p-values >0.10). In diabetic patients, at least one adverse event occurred in 16%, 23%, 23% and 33% of patients on placebo, ranolazine 500 mg, 1000 mg and 1500 mg, respectively; in non-diabetic patients the analogous values were 15%, 13%, 21% and 34%, respectively. Mean changes (±SE) from baseline to the end of the study in glucose and triglyceride levels were similar between diabetics and non-diabetics (change in glucose: diabetics 10±11 mg/dL, non-diabetics 3±2 mg/dL [NS]; change in triglycerides: diabetics 10±17mg/dL, non-diabetics -7±6 mg/dL [NS]). **Conclusion:** Patients with chronic angina and diabetes appear to tolerate and to respond to ranolazine, a pFOX inhibitor, as well as patients without diabetes.

Exercise Duration* (seconds)

Treatment	Placebo		Ranolazine 500 mg bid		Ranolazine 1000 mg bid		Ranolazine 1500 mg bid	
	troug h	peak	trough	peak	trough	peak	trough	peak
Diabetics n=42	499	498	520	527	526	550	530	547
Non-diabetics n=133	503	500	528	530	539	550	554	557

*Values are given as least squares means. Treatment p-values: trough <0.001, peak <0.001; treatment by diabetes interaction p-values: trough p=0.768, peak=0.953

1152-93 Prolonged Statin Therapy and the Arterial Elasticity in Stable Coronary Artery Disease

Magorzata Kurpesa, Ewa Trzos, Micha Kidawa, Maria Krzemińska-Pakua, Zbigniew M. Bednarkiewicz. *Medical Academy, £ódŸ, Poland*

Background: Hypercholesterolemia and atherosclerosis are known to influence the mechanical properties of the arterial tree. Statins may alter the arterial distensibility because they decrease plasma cholesterol level and inhibit the progression of atherosclerosis. Pulse wave velocity (PWV) provides an indirect, non-invasive measurement of mechanical properties of the arteries. The aim of the study was to evaluate the influence of statin therapy on arterial elasticity in pts with coronary artery disease(CAD). **Methods:** Study group consisted of 46 pts with angiographically documented, clinically stable CAD and with high-normal plasma cholesterol level(190-210 mg/dl). They were randomised into Group I-23 pts who received placebo and Group II-23 pts who received statin therapy. Groups were comparable according to age, gender, risk factors and treatment of

CAD. Before and following 6 months of treatment PWV was evaluated using a computer system COMPLIOR. In each patient carotid-femoral PWV was measured. For automatic measurement of PWV pressure waveforms were digitized at rate 500Hz for carotid-femoral distance.10 healthy volunteers constituted a control group. **Results:** After 6 months the plasma cholesterol level was 205±21mg/dl in Group! and 168±15 mg/dl in Group II(p<0,01). Results of PWV are shown in the table.*p<0,01

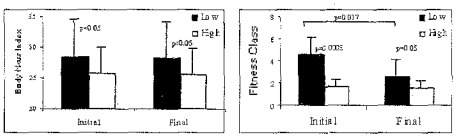
	Pulse wave velocity m/s		
	Group I	Group II	Control
Initial	12,1 ± 1,3	12,3 ± 0,8	7,0 ± 0,6
After 6 months	12,4 ± 2,0	8,9 ± 0,7*	7,2 ± 0,4

After 6-month therapy with statin a significant decrease of PWV was observed. This result may be explained by beneficial effect of statins on the degree of plaque growth. The alternative explanation may be the influence of statins on vascular remodeling. **Conclusion:** Statin therapy may improve arterial elasticity in patients with normal plasma cholesterol and stable CAD.

1152-94 Relation Between Self-Efficacy and Diet/Exercise Adequacy in Cardiac Rehabilitation

Sammy Chan, Kori Kingsbury, Frances Johnson, Anka Brozic, Wolfgang Linden, Sandra Barr, Jiri Frohlich, Andrew Ignaszewski. *University of British Columbia, Vancouver, BC, Canada*

Background: Self-efficacy (SE) has been shown to influence health behavior. To determine the role of SE in cardiac rehabilitation (CRP), we correlated SE with measures of diet/exercise compliance in participants of CRP. **Methods:** 47 subjects (age 61±13, 19% female, 68% CAD) were evaluated. SE was judged in 2 domains (diet, exercise) with a SE questionnaire (SEQ) using Likert scales. Adequacy of diet was assessed with body mass index (BMI). Adequacy of exercise was assessed with age adjusted fitness classification (FIT) (1-7, most to least fit) based on treadmill results. SEQ was tested prior to CRP. BMI and FIT were measured prior to and at completion. All subjects completed a 4 month CRP with supervised exercise conditioning and outpatient diet counseling. **Results:** Subjects were divided into 2 groups based on their SEQ scores. At initial evaluation, subjects with high dietary SE had a significantly lower BMI (figure). The indices did not change in either group at completion. Exercise SE was evaluated in subgroup with negative stress test. At start of CRP, subjects with high exercise SE were significantly more fit (figure). However, subjects with low SE improved significantly during CRP while there was no change in FIT in subjects with high exercise SE scores. **Conclusions:** (1) diet and exercise SEQ scores correlate with initial BMI and FIT suggesting that these scores are useful in predicting behavior in an ambulatory setting; (2) a supervised exercise CRP improves FIT especially in subjects with low SE; (3) dietary counseling only has a minimal impact on BMI regardless of SE.



POSTER SESSION

1153 Time to Treatment in Acute Myocardial Infarction

Monday, March 19, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 4:00 p.m.-5:00 p.m.

1153-95 Emergency Transfer of District and Rural Hospital Acute Myocardial Infarct Patients for Immediate Angiography ± Intervention Is Associated With Excellent Clinical Outcomes Despite a High Risk Population and Long Transport Delays

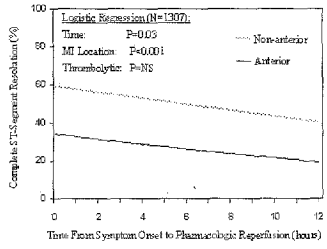
Peter Hansen, Yutaka Koyama, Michael Ward, Helge Rasmussen, Greg Nelson. *Royal North Shore Hospital, Sydney, Australia*

Background: District (D) and rural (R) hospital patients (pts) with acute myocardial infarction (MI) in whom fibrinolytic therapy (FT) fails or is contraindicated (C/I) have a high in-hospital morbidity and mortality. Limited information is available on emergency transfer to a tertiary centre for immediate coronary angiography (CA)/intervention. **Methods and Results:** Between 7/1997-9/2000 we prospectively examined in-hospital outcomes of 142 consecutive MI pts from D and R hospitals with FT failure (75%) or C/I (25%) urgently transferred to Royal North Shore (RNS) a tertiary centre for immediate CA/intervention. Average transfer distance ± SD was 68 km ± 19 km. Pt arrival was "out of hours" in 66%. Mean age was 63±13 yrs (range: 28-88 yrs) and F:M ratio 4:9. Previous MI, percutaneous transluminal coronary intervention (PTCA), coronary artery bypass grafting (CABG), cerebrovascular accident (CVA) and diabetes was present in 18%, 6%, 8%, 8% and 15% respectively and 30% of pts were Killip class III/IV. Mean time from diagnostic ECG to RNS notificatioon and from RNS notification to pt arrival was 294 and 115 min respectively. At CA 75% had TIMI 0, 1 or 2 flow in the infarct related artery. TIMI 3 flow was established in 88% at a mean of 61 min after RNS arrival. Treatment included: stenting 63%, PTCA 9%, emergency CABG 10%, in-hospital CABG 8% and no intervention 10%. Reopro was used in 33% and intraaortic balloon pumping in 27%. In-hospital mortality was 8.3% with reMI, CVA and target lesion revascularisation in 1.7%, 2.5% and 8.3% respectively. Mean total D/R+RNS hospital stay was 8.3 ± 1.1 days. **Conclusion:** Emergency transfer of MI patients from D and R hospitals with FT failure or C/I to a tertiary centre for immediate CA ± revascularisation results in an excellent short-term outcome despite a high-risk population and long transport delays.

1153-96 Relation Between Time-to-Pharmacologic Reperfusion and the Probability of Achieving Complete ST-Segment Resolution in ST Elevation Myocardial Infarction

Howard A. Cooper, James A. de Lemos, Sabina A. Murphy, Carolyn H. McCabe, Kristin C. Schuhwerk, Elliott M. Antman, Eugene Braunwald. *Brigham and Women's Hospital, Boston, MA*

Background: ST-segment resolution reflects myocardial reperfusion and predicts mortality following ST elevation MI. The relation between time-to-pharmacologic reperfusion and ST-segment resolution is unknown.
Methods: Data were pooled for 544 patients randomized to various combinations of reteplase, alteplase, and abciximab (TIMI 14 trial) and 763 patients randomized to full-dose lanoteplase or alteplase (InTIME II trial). Multivariable logistic regression was used to assess the independent relation between time from symptom onset to the start of pharmacologic reperfusion and the probability of achieving complete (≥70%) ST-segment resolution at 90 minutes. Other variables in the model were infarct location (anterior/non-anterior), abciximab use in TIMI 14 (yes/no), and fibrinolytic agent (alteplase/reteplase/lanoteplase).
Results: Time-to-treatment was inversely related to the probability of achieving complete ST-segment resolution at 90 minutes (per hour OR 0.94, 95% CI 0.89-0.99, p=0.03). Patients with non-anterior infarcts were more likely to achieve complete ST-segment resolution (OR 2.81, 95% CI 2.21-3.57, p<0.001). The probability of achieving complete ST-segment resolution was not significantly different among the 3 fibrinolytic agents (p=NS), but was greater if abciximab was part of the reperfusion regimen (OR 2.05, 95% CI 1.51-2.78, p<0.001).
Conclusion: While the effects of abciximab and infarct location predominate, time-to-treatment also has a significant impact on the probability of achieving reperfusion at the myocardial level. This may be one mechanism by which earlier pharmacologic reperfusion results in reduced mortality in ST elevation MI.



1153-97 Prehospital Infarction Angioplasty Triage (PHIAT): Results From the Zwolle Myocardial Infarction Study Group

Nicolette Ernst, Menko Jan de Boer, Arnoud W. J. van 't Hof, Frans Hollak, Jan C. A. Hoorntje, Harry Suryapranata, Jan Henk E. Dambrink, Felix Zijlstra. *Isala Klinieken, hospital De Weezenlanden, Zwolle, The Netherlands*

Background: Time from onset of symptoms to reperfusion therapy is of paramount importance for the clinical outcome in patients (pts) with acute myocardial infarction (AMI). Prehospital identification of pts with AMI may result in a reduction of total ischemic time when considering primary angioplasty (PA) treatment. **Methods:** Between November 1998 and July 2000, 17 ambulances were equipped with 12-lead ECG computers using an algorithm to identify large AMI. When pts were identified as having large AMI, immediate transfer and preparation of cath lab and personnel were initiated. **Results:** During the study period in 213 pts the indication for PA treatment was made. The mean age was 60.4 years (range 16-90). One patient died before arrival in the hospital.

Clinical characteristics (n=212):

	N	%
Male	160	75
Previous MI	23	11
Immediate angiography	210	99
Anterior MI	89	45
No AMI, other diagnosis	12	6
PA (N=191) success	177	93
Urgent bypass surgery	2	1
Bypass surgery later	17	8

The median time from symptom onset to admission and from admission to first balloon inflation were 122 and 38 minutes respectively. The total mortality with a mean follow-up of 6 months was 6%. **Conclusion:** Pre-hospital triage in the ambulance is a feasible, effective and safe way to identify patients with large AMI in order to transfer them directly

to a center for primary angioplasty. A considerable amount of patients (6%) do not have a myocardial infarction and this is definitely more than is reported from prehospital thrombolysis trials.

1153-98 Delayed Is Better Than Early Elective Intervention After Acute Myocardial Infarction Treated With Thrombolytic Therapy

Abid R. Assali, Ali Moustapha, Stefano Sdringola, Joseph Salloum, Mohammad Ghani, Sangeeta Saikia, Susan Hale, Goerge Schroth, Oscar Rosales, Vernon H. Anderson, Richard W. Smalling. *UNIVERSITY OF TEXAS MEDICAL SCHOOL AND HERMANN HOSPITAL, HOUSTON, TX*

Background: Optimal timing of elective percutaneous coronary intervention (PCI) after acute myocardial infarction (MI), especially those treated with thrombolytic therapy (TT), is unknown. **Aims:** We compared the results of early (6-24 hours) and delayed (>24 hours) elective PCI in acute MI patients (pts) treated with TT. **Methods:** We performed a retrospective analysis of 231 consecutive pts with acute MI undergoing elective PCI after successful TT (pts undergoing emergency PCI or hemodynamic instability were excluded): Group I = 86 pts (37%), 6-24hours; Group II = 145 pts (63%), >24hours. Each group was analyzed according to TT. All major adverse cardiac events (MACE: death, non-fatal MI, and re-intervention) were recorded.

	GROUP I (24>TIME>6 hours)		Group II (Time> 24 hours)		P-value
	TT+	TT-	TT+	TT-	
# Patients	12	74	30	115	
AGE (YRS)	57-/+13	56-/+12	59-/+13	58-/+14	0.4
DM	3 (25%)	25 (34%)	5 (17%)	37 (32%)	0.1
1-Vessel disease	10 (83%)	53 (72%)	22 (73%)	84 (73%)	0.6
Anterior MI	3 (25%)	32 (43%)	9 (30%)	43 (38%)	0.3
Stent	7 (58%)	30 (41%)	29 (97%)	90 (78%)	0.005
GP2b/3a	3 (25%)	38 (51%)	7 (21%)	32 (28%)	0.8
In-hospital death	1 (8.2%)	0 (0%)	0 (0%)	2 (1.2%)	0.5
In-hospital MACE	3 (25%)	5 (7%)	0 (0%)	11 (10%)	0.02

Conclusion: Early (6-24 hours) elective PCI after acute MI is associated with higher rate of in-hospital MACE especially when thrombolytic therapy was given.

1153-99 Influence on Outcome of Time From Myocardial Infarction Onset to Primary Angioplasty

Thierry Lefevre, Christophe Loubeyre, Marie-Claude Morice, Yves Louvard, François Gobeil, Rajpal Abhaichand, Jean-François Piéchaud. *ICPS, Massy, France*

Background: Time from MI onset to thrombolysis has been shown to be a predictive factor of procedure failure and mortality. The same influence of time to primary PTCA (TIME) on patient outcome still remains controversial.
Methods: We retrospectively assessed from our AMI database (January 1995 to December 2000) the influence of TIME on angiographic results and in-hospital outcome. All pts admitted for acute MI were included. The strategy was as follows: direct admission to the cath-lab for immediate coronary angiogram, PTCA and stent implantation when indicated and feasible.
Results: During this period, 1030 pts were admitted ≤ 12 hours. Time from admission to reperfusion was 41.9±44.6 min. The main pts characteristics and results according to TIME are summarized below

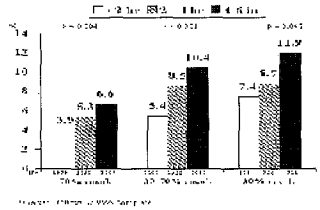
	Time (hours)	3.1-6	6.1-9	9.1-12	p
Patients (%)	39	39	13	10	-
Female Gender (%)	20	21	17	28	ns
Previous MI (%)	18	11	6	6	<0.01
Age (yr)	59+/-14	64+/-14	60+/-14	62+/-16	<0.05
Anterior MI (%)	49	45	42	49	ns
Prehospital Thrombolysis (%)	14	19	24	13	ns
Killip 3or 4 (%)	14	14	12	15	ns
Stent used (%)	90	89	92	86	ns
Final TIMI 3 (%)	94	91	89	80	<0.01
Angiographic success (%)	97	98	99	95	ns
Death (%)	6.6	6.7	10.2	10.1	<0.05

Conclusion: In this observational study including all AMI pts ≤ 12 hours, the majority were admitted less than 6 hours after MI onset. Patients admitted earlier were younger and had more frequently a previous MI. In our series this earlier treatment led to higher final TIMI 3 rate and lower mortality.

1153-100 Time to Treatment Influences the Impact of ST Segment Resolution on One Year Prognosis: Insights From ASSENT-2

Yuling Fu, Shaun Goodman, Wei-Ching Chang, Padma Kaul, Frans Van de Werf, Christopher B. Granger, Paul W. Armstrong, for the ASSENT 2 Investigators. *University of Alberta, Edmonton, AB, Canada*

Rapid resolution of ST-segment elevation at 90 and 180 min following fibrinolytic therapy is related to early coronary artery patency and improved clinical outcomes in patients with acute myocardial infarction(AMI). However the prognostic value of later ST resolution assessed at 24 hours in predicting 1-year mortality is unknown. Moreover the impact of time to treatment on extent of 24-hour ST resolution has not been previously evaluated. Accordingly, we studied these issues using Schröder's method in ASSENT-2 where 13045 patients had both baseline and 24-hr ECGs free of confounders (LBBB, ventricular rhythm, reinfarction). Of these patients, 50% had complete resolution(>70%), 36% had partial resolution(30-70%), and 14% had no ST resolution(< 30%). The overall 1-year mortality rates for these patients were 5.1%, 8.1%, and 9.5%, respectively (p< 0.001). Analysis according to pre-specified time windows revealed complete ST resolution in 54.7 % of patients treated within 2 hours, in 50.6% treated between 2 - 4 hours, and in 42% treated between 4 - 6 hours (p < 0.001). The figure shows 1-year mortality partitioned according to extent of ST resolution and time to treatment. The extent of ST resolution was inversely associated with time to treatment. Indeed, within each category of ST resolution, the sooner the patients were treated, the lower their mortality. Hence irrespective of the extent of ST resolution, incorporating time to treatment provides additional prognostic value. These results further emphasize the importance of early treatment for AMI.



POSTER SESSION

1154 Specific Clinical Risk Markers in Acute Coronary Syndromes

Monday, March 19, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 4:00 p.m.-5:00 p.m.

1154-75 Diabetes Mellitus Prevents Ischemic Preconditioning by Prodromal Angina in Patients With a First Anterior Wall Acute Myocardial Infarction

Masaharu Ishihara, Hikaru Sato, Takuji Kawagoe, Yuji Shimatani, Satoshi Kurisu, Kenji Nishioka, Yasuyuki Kouno, Takashi Umemura, Shuji Nakamura. *Hiroshima City Hospital, Hiroshima, Japan*

Background: Prodromal angina occurring shortly before the onset of acute myocardial infarction is associated with favorable outcome by the mechanism of ischemic preconditioning. However, little is known about impact of diabetes on ischemic preconditioning. **Methods:** We studied 620 consecutive patients with a first anterior wall acute myocardial infarction who underwent emergency catheterization with 12 hours after the onset of chest pain. Prodromal angina was defined as angina episode(s) occurring within 24 hours before the onset of acute myocardial infarction. Serial contrast left ventriculograms were obtained in 505 patients at the time of acute and predischarge catheterization. **Results:** In 490 patients without diabetes, prodromal angina was associated with lower peak creatine kinase value (3,068±2,647IU/L vs 3,601±2,462IU/L, p=0.037), more improvement of left ventricular ejection fraction (9.7±13.2% vs 5.6±13.6%, p=0.0095) and lower in-hospital mortality (3.4% vs 9.3%, p=0.015). On the contrary, in 130 diabetic patients, there was no significant difference in peak creatine kinase value (3,382±2,520IU/L vs 3,233±2,412IU/L, p=0.75), the change in left ventricular ejection fraction (7.2±14.0% vs 8.2±15.1%, p=0.76) and in-hospital mortality (8.8% vs 11.0 %, p=0.68) between patients with and those without prodromal angina. **Conclusion:** Prodromal angina occurring shortly before the onset of acute myocardial infarction was associated with limited infarct size, enhanced recovery of left ventricular function and improved survival. However, such beneficial effects of prodromal angina were not observed in diabetic patients, suggesting that diabetes might prevent ischemic preconditioning in patients with acute myocardial infarction.

1154-76 Association of Chronic Renal Insufficiency With Adverse Cardiovascular Outcome After Acute Coronary Syndrome: A Study From the Michigan Cardiovascular Outcomes Research and Reporting Program

Rosario V. Freeman, Rajendra H. Mehta, Jeanna Cooper, Eva Kline-Rogers, Kim A. Eagle. *University of Michigan, Ann Arbor, MI*

Background: In order to address the association of chronic renal insufficiency (CRI) (serum creatinine >1.5 mg/dl) with known cardiovascular risk factors and mortality among patients admitted with acute coronary syndromes, 925 consecutive patients presenting with an acute coronary syndrome to a tertiary academic medical center in 1999 were studied. **Methods:** Demographic, procedural, and outcome data were collected prospectively on a standardized data collection form. Predictors of in-hospital mortality were identified by univariate analysis. Odds ratios (OR) and 95% confidence intervals (CI) for in-hospital mortality were calculated. Multivariate logistic regression was used to

assess the independent association of CRI with in-hospital mortality. **Results:** 176 patients (19.0%) had CRI. Overall, there were 43 in-hospital deaths (4.6%), of which 27 were in CRI patients. Patients with CRI were older and had more prior congestive heart failure, diabetes, hypertension and myocardial infarction (table). CRI patients had longer hospital stays, were less likely to have a normal angiogram and were more likely to have a failed procedure if coronary intervention was attempted. CRI was an independent predictor of in-hospital mortality.(OR 7.02, 95% CI 3.5 to 13.9 p<0.0001), after adjustment for older age, presence of congestive heart failure and diabetes. **Conclusions:** CRI is prevalent in patients presenting with an acute coronary syndrome and is an under-appreciated independent risk factor for in-hospital mortality. Recognition of the increased risk burden of CRI identifies a patient subset at substantially higher risk of adverse cardiovascular outcome.

	CRI	NON-CRI	p-value
DEMOGRAPHICS	N=176	N=749	
Age	67+/-14	63+/-14	<0.0001
Male(%)	115(65)	481(64)	0.57
Hypertension(%)	135(77)	455(61)	<0.0001
Diabetes Mellitus(%)	87(49)	192(26)	<0.0001
CHF(%)	83(47)	98(13)	<0.0001
PreviousMI(%)	98(56)	325(43)	<0.0001
Ejection Fraction	41+/-16	50+/-17	<0.0001
OUTCOMES			
Days Admitted	5.9+/-5.2	4.9+/-6.0	0.01
Failed Procedure	4 of 41 PCIs	11 of 295 PCIs	0.04
Non Q-wave MI	66(38)	233(31)	0.05
Major Bleeding	24(14)	76(10)	0.09
Normal Angiogram	5(3)	455(61)	<0.0001
In-Hospital Death	27(15)	16(2)	<0.0001

1154-77 Atrioventricular Nodal Block in Acute Myocardial Infarction Treated With Thrombolytic Therapy Is Common and Portends Poor Prognosis: Results From Large Trials of Thrombolytic Therapy

Sana M. Al-Khatib, E. Magnus Ohman, Harvey D. White, Christopher B. Granger, Robert M. Califf, Rakhi Kilaru, Eric J. Topol. *Duke Clinical Research Institute, Durham, NC*

Background: In the pre-thrombolytic era, atrioventricular nodal block complicating acute myocardial infarction was associated with a poor prognosis. The incidence and prognosis of atrioventricular nodal block in the setting of acute myocardial infarction treated with thrombolytic therapy are less well defined. We examined the incidence, predictors, and outcomes of second and third degree atrioventricular nodal block in 76,002 patients with ST-segment elevation myocardial infarction treated with thrombolytic therapy enrolled in the GUSTO-I, GUSTO-IIb, GUSTO-III, and ASSENT-II trials. **Methods:** We compared baseline characteristics and 30-day mortality of patients with atrioventricular nodal block (5,273) to those without it (70,729). **Results:** The incidence of atrioventricular nodal block was 7.5%. Significant predictors of atrioventricular nodal block were inferior myocardial infarction location (Odds Ratio [OR] 2.9, 95% Confidence Interval [CI] 2.7-3.1), history of congestive heart failure (OR 2.4, 95% CI 2.3-2.6), female gender (OR 1.5, 95% CI 1.4-1.6), Killip class at presentation (OR 1.4, 95% CI 1.4-1.5), and older age (OR 1.2, 95% CI 1.2-1.3). In a time-dependent analysis, patients with atrioventricular nodal block had a significantly higher 30-day mortality (20% versus 6%, p-value 0.001). **Conclusion:** Atrioventricular nodal block is a relatively common and understudied complication of acute myocardial infarction and is associated with a poor prognosis even when thrombolytic therapy is used. The related use of treatments, including pacemakers and beta-blockers, needs further study.

1154-78 Ischemic Burden in the Standard ECG Identifies Patients Who Benefit Most From an Early Invasive Strategy in Unstable Coronary Artery Disease: A FRISC2 Substudy

Lene Holmvang, Peter Clemmensen, Bertil Lindahl, Bo Lagerqvist, Per Venge, Lars Wallentin, Peer Grande. *The National University Hospital, Copenhagen, Denmark, Uppsala University Hospital, Uppsala, Sweden*

Background: Ischemic burden, defined as amount of ST-segment depression in the ECG has been shown to relate to prognosis in patients with acute coronary syndromes. **Methods:**We evaluated the influence of the iscemic burden on the effects of an early invasive versus a conservative treatment strategy in the FRISC 2 trial as well as the relationship between ischemic burden and Troponin T values and angiographic findings at day 5-7. 2210 patients with chest pain and signs of ischemia (ST-depression, T-wave inversion and/or elevated biochemical markers) were included. The inclusion ECG was evaluated regarding ST-segment deviation (>0.05mV) and the summed ST-segment deviation in 11 leads (except aVR) was calculated. Patients with bundle branch block, fascicular block and left ventricle hypertrophy constituted a separate subgroup of 514 patients.

Summed ST-segment deviation	Non-invasive strategy Death, MI 1 year	Invasive strategy Death, MI 1 year	p (Chi2)	Troponin T (ug/L)median values	Ptts w. LMS, 2VD or 3 VD (only invasive group)
0-2.5mm	9.3%	11.7%	0.45	0.09	43.9%
3-5.5mm	13.3%	6.2%	0.004	0.15**	54.3%*
>=6mm	19.4%	9.5%	0.002	0.23**	68.3%**
ECG confounders	15.5%	13.4%	0.57	0.21	61.7%

*p<0.05 or **p<0.01 compared with group above. **Results:**An invasive treatment strategy reduced the risk of death or AMI by 1 year follow up significantly in the subgroups with the highest degree of ischemia.There was a gradual increase in Troponin T values by an increasing level of ischemic burden as well as the patients with the most ST-segment deviation had more severe coronary artery disease by 5-7 days angiography. **Conclusion:** In patients with unstable coronary artery disease the ischemic burden determined by ECG is related to poor outcome in patients treated non-invasively. An invasive treatment strategy provides a significant risk reduction in these patients.In addition, ischemic burden in the ECG is also correlated to Troponin T level and to the severity of coronary artery disease by angiography.

1154-101 Emergency Department Rest Myocardial Perfusion Imaging Results in More Effectve Utilization of Coronary Angiography in Low Risk Chest Pain Patients

Michael C. Kontos, Rakesh K. Shah, Kristin L. Schmidt, RObert L. Jesse, Joseph P. Ornato, James L. Tatum. *MCV/VCU, Richmond, VA*

Background: Previous studies have shown that using myocardial perfusion imaging (MPI) with sestamibi in Emergency Department (ED) patients (pts) with chest pain is cost effective. This may result from more effective utilization of invasive testing, with a reduction of coronary angiography in low-risk pts. **Methods:** We compared a consecutive group of pts prospectively evaluated according to a protocol using MPI in low risk pts (ACT) to a control group (CON) evaluated during the year prior to implementation of the protocol. CON patients were retrospectively assigned a pre-defined risk level based on the ED admission record and ECG. High risk (High) unstable angina pts were compared to lower risk pts (Low), who underwent ED MPI in the ACT group but not in the CON group, to assess the relationship of MPI to the use of coronary angiography (Cath), presence of significant disease (Sig Dz [>70% stenosis]), and revascularization (Rev) in tests performed within 30 days of ED evaluation. **Results:** There was no difference in the proportion of pts who were High and Low risk between the two groups (table). High risk CON pts underwent stress testing more frequently (p<0.05) than did High risk ACT pts. Cath was performed as frequently in High risk CON and ACT pts, with no difference in the incidence of Sig Dz and Rev. In contrast, Cath was performed less frequently in Low risk ACT pts (p<0.05), but the yield was higher, with more Sig Dz (p<0.005) and Rev (p<0.05). There was no significant difference in costs between the ACT and CON groups, either in the High risk ($9435 vs $10,425) or Low risk ($2800 vs 2896) pts. **Conclusions:** The higher proportion of Sig Dz and Rev in ACT pts suggests more appropriate invasive test utilization in Low risk chest pain pts. ED MPI improves cost effectiveness of Low risk pts by increasing the yield of invasive testing.

	% Pts	% Stress	% Cath	% Sig Dz	% Rev
CON, High (n=175)	27	24	45	72	59
ACT, High (n=198)	25	16 *	50	59	45
CON, Low (n=464)	73	21	19	31	22
ACT, Low (n=597)	75	53 **	13 *	51 **	38 *

* =p<0.05; ** =p<0.005

1154-102 Outcome of Patients With Acute Coronary Syndromes With and Without Prior CABG: Results From the PURSUIT Trial

Marino Labinaz, Rakhi Kilaru, Karen Pieper, Steven P. Marso, Lisa Berdan, Michael Kitt, Maarten L. Simoons, Robert M. Califf, Eric J. Topol, Robert A. Harrington, Paul W. Armstrong, for the PURSUIT Investigators. *University of Ottawa Heart Institute, Ottawa, ON, Canada, Duke University Medical Center, Durham, NC*

Coronary Artery Bypass Grafting (CABG) signifincantly improves the morbidity and mortality of patients (pts) with advanced coronary artery disease. However, it is unclear whether prior CABG protects pts presenting with acute coronary syndromes (ACS) from adverse events. Furthermore, the effect of glycoprotein (GP) IIb/IIIa blockade in pts with prior CABG presenting with ACS is also unknown. The purpose of this study was to evaluate the baseline characteristics and outcomes of pts presenting with ACS with and without prior CABG. **Methods:** PURSUIT randomized pts presenting with ACS to 72 hrs of treatment with the GP IIb/IIIa antagonist eptifibatide (ept) vs placebo. **Results:** In PURSUIT, 1134 pts (12.0%) had prior CABG. Pts with prior CABG were older, heavier, had significantly more cardiac risk factors, more prior MI, stroke, PVD and PTCA compared to pts without prior CABG. The use of aspirin, beta-blockers, calcium channel blockers, ACE inhibitors and nitrates were higher in the 2 wks prior to presentation in pts with prior CABG. The incidence of death and death/MI in prior CABG compared to non-prior CABG at 30 days was 5.2 vs 3.4% and 15.7 vs 14.8% and at 6 months it was 8.1 vs 6.1% and 20.7 vs 18.1%. The table shows adjusted hazard ratios (95% CI) for death and death/MI by prior CABG. Comparing ept vs placebo in pts with prior CABG, the 30 day mortality was 4.1 vs 6.3%; 30 death/MI was 15.0 vs 16.5%. **Conclusions:** Pts presenting with ACS and prior CABG have significantly worse baseline characteristics than non-prior CABG pts. Prior CABG pts have significantly higher mortality at 30 days and 6 months

despite adjusting for differences in baseline characteristics and treatments. The treatment effects of ept among prior CABG pts were consistent with the overall PURSUIT trial.

Outcomes in Patients with prior CABG vs No prior CABG

Event	Adjusted Hazard Ratio (95%CI)	P-value
Death (30 day)	1.45 (1.06-1.98)	0.019
Death (6 mos)	1.32 (1.04-1.67)	0.021
Death/MI (30 day)	0.95 (0.80-1.13)	0.55
Death/MI (6 mos)	1.02 (0.88-1.19)	0.78

ORAL CONTRIBUTIONS

838 Combination Strategies for Managing Acute Myocardial Infarction

Monday, March 19, 2001, 4:00 p.m.-5:30 p.m.
Orange County Convention Center, Room 230D

4:00 p.m.

838-1 A Prospective, Multicenter, International Randomized Trial Comparing Four Reperfusion Strategies in Acute Myocardial Infarction: Principal Report of the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) Trial

Gregg W. Stone, Cindy L. Grines, David A. Cox, Eulogio Garcia, James E. Tcheng, Thomas Stuckey, John Carroll, Giulio Guagliumi, Barry Rutherford, Gary Johnson, Mark Effron, Paolo Esente, Alexandra J. Lansky, John Griffin. *The Cardiovascular Research Foundation and Lenox Hill Heart and Vascular Institute, New York City, NY*

Background: Prior studies have shown that stent implantation in AMI, while reducing recurrent ischemia and restenosis compared to PTCA alone, may degrade antegrade blood flow and result in increased mortality. These studies were done with first generation stent technology, and without the routine use of GP IIb/IIIa inhibitors. **Methods:** To determine the optimal reperfusion strategy in AMI, 2082 pts of any age with AMI <12 hrs without cardiogenic shock were randomized at 76 sites to primary PTCA alone (n=516), PTCA with abciximab (n=529), stenting alone (n=512), or stenting with abciximab (n=525), and followed for 12 mos. The stent used was the MultiLink and MultiLink Duet. Angiographic inclusion criteria included native ref. vessel dia. >2.5 mm or <4.5 mm, lsn length <65 mm, non-ostial location, and absence of major side branch involvement. The primary endpoint was the 6 mo composite incidence of death, disabling stroke, reinfarction, and ischemic TVR. Protocol 6 mo angiographic follow-up was performed in a 962 pt subset to assess myocardial recovery and restenosis. **Results:** Mean age was 60 + 12 yrs (range 21-95), 27% were female, 17% had diabetes, and 37% had anterior MI. Median time from symptom onset to ER was 1.8 hrs, and from ER to PTCA 2.0 hrs. By core lab analysis, TIMI-3 flow was restored in 95.3% of pts after PTCA, 96.3% after PTCA + abciximab, 94.6% after stenting, and 96.1% after stent + abciximab (all p=NS). The primary clinical endpoint data appear in the table

6 Month Events

	PTCA	PTCA + Abciximab	Stent	Stent + Abciximab
Death	4.3%	2.3%	2.7%	3.8%
Disabling stroke	0.2%	0%	0.2%	0.6%
Reinfarction	1.6%	2.1%	1.2%	2.3%
Ischemic TVR	14.0%	11.9%	7.2%††	5.0%‡‡
MACE	18.4%	14.2%*	10.4%†	9.5%‡

*p=0.06 vs. PTCA alone; †p=0.0002 vs. PTCA alone; ‡p=0.02 vs. PTCA + abciximab; ††p=0.0005 vs. PTCA alone; ‡‡p<0.0001 vs. PTCA + abciximab.

Conclusions. Compared to primary PTCA alone, MultiLink stent implantation during AMI results in a marked reduction in ischemic TVR and MACE at 6 mos, without adversely affecting TIMI flow or survival. The outcomes tend to be further improved with abciximab, especially in pts undergoing PTCA alone. Complete 12 mo clinical results, and 6 mo angiographic data will be presented for the first time in March.

4:15 p.m.

838-2 Does Stenting and Glycoprotein IIb/IIIa Receptor Blockade Improve the Prognosis of Diabetics Undergoing Primary Angioplasty in Acute Myocardial Infarction? The CADILLAC Trial

Thomas Stuckey, Cindy L. Grines, David A. Cox, Eulogio Garcia, James E. Tcheng, John Carroll, Barry Rutherford, Giulio Guagliumi, Paolo Esente, Alexandra J. Lansky, John Griffin, Gregg W. Stone. *The Cardiovascular Research Foundation and Lenox Hill Heart and Vascular Institute, New York City, NY, Moses Cone Memorial Hospital, Greensboro, NC*

Background. Although the prognosis of pts with AMI and diabetes mellitus (DM) is improved with primary PTCA compared to thrombolytic therapy, long-term outcomes are still poor compared to non-DM. Patients with DM undergoing elective PCI may benefit by stent implantation (reduced TVR) and abciximab (Abx; prolonged survival). **Methods.** To examine whether similar benefits of stents and Abx are conferred in an AMI population, we examined the CADILLAC database, in which 2,082 pts of any age with AMI <12 hrs in duration without cardiogenic shock were randomized to primary PTCA, PTCA + Abx, stenting with the MultiLink or MultiLink Duet stent, or stenting + Abx. DM was present in 346 pts (16.6%). The primary clinical endpoint was the 6 month composite incidence of death, disabling stroke, reinfarction and ischemia requiring TVR. **Results.** Compared to non-DM pts, the 6 month rate of MACE was increased in the diabetic (17.1% vs. 12.3%, p<0.02). Considering the individual components of the primary endpoint, death occurred in 4.9% of pts with DM vs. 2.9% of pts without DM(p=0.06); disabling stroke occurred in 0.3% vs. 0.2% respectively (p=0.99); reinfarction 2.0% vs. 1.7% (p=0.70); and ischemic TVR 11.9% vs. 10.2% (p=0.037). The outcomes in DM and non-DM stratified by treatment appear in the table:

6 Month Results

Diabetics	All PTCA (n=162)	All Stent (n=184)	No abciximab (n=162)	Abciximab (n=184)
Death	3.7%	6.0%	3.7%	6.0%
Disabling stroke	0%	0.5%	0.6%	0%
Reinfarction	2.5%	1.6%	1.9%	2.2%
Ischemic TVR	17.3%	7.1%*	13.0%	10.9%
MACE	20.4%	14.1%**	17.3%	16.8%
Non-diabetics	**All PTCA (n=883)**	**All Stent (n=853)**	**No abciximab (n=866)**	**Abciximab (n=870)**
Death	3.2%	2.6%	3.5%	2.4%
Disabling stroke	0.1%	0.4%	0.1%	0.4%
Reinfarction	1.7%	1.8%	1.3%	2.2%
Ischemic TVR	12.1%	5.9%†	10.2%	7.9%††
MACE	15.5%	9.0%†	13.9%	10.8%‡

*p=0.0003 vs. all PTCA; **p=0.12 vs. all PTCA; †p<0.0001 vs. all PTCA; ††p=0.11 vs. no Abx; ‡p=0.053 vs. no Abx.

Conclusions. Stent implantation in pts with AMI, compared to PTCA alone, significantly reduces ischemic TVR within 6 months in both pts with diabetes (31% relative risk reduction) and non-diabetes (51% reduction). A potential benefit of abciximab in reducing MACE at 6 months was evident in non-diabetic pts, but not in those with diabetes.

4:30 p.m.

838-3 Effect of Stent Implantation and Glycoprotein IIb/IIIa Receptor Blockade on TIMI Flow and Mortality After Primary PTCA in Acute Myocardial Infarction: Final Results of the CADILLAC Trial

Cindy L. Grines, David A. Cox, James E. Tcheng, Eulogio Garcia, Thomas Stuckey, John Carroll, Giulio Guagliumi, Barry Rutherford, Paolo Esente, Alexandra J. Lansky, John Griffin, Gregg W. Stone. *The Cardiovascular Research Foundation and Lenox Hill Heart and Vascular Institute, New York City, NY, William Beaumont Hospital, Royal Oak, MI*

Background. Long-term mortality after reperfusion therapy in AMI is directly related to the early achievement of TIMI-3 flow. In the randomized Stent PAMI Trial, post procedural TIMI –3 flow rates were reduced in Palmaz-Schatz stented pts compared to those undergoing PTCA only, which resulted in a strong trend toward increased mortality after stenting, offsetting the benefit of reduced restenosis. However, GP IIb/IIIa inhibitors were rarely used in Stent PAMI, and lower profile, better performing stents have since been introduced. **Methods.** To determine the optimal reperfusion strategy in AMI, 2,082 pts of any age with symptom duration <12 hrs without cardiogenic shock were randomized at 76 international centers in a 2x2 factorial design to primary PTCA alone (n=516), PTCA + abciximab (n=529), stenting with the MultiLink or MultiLink Duet stent (n=512), or stenting + abciximab (n=525). **Results.** By core lab analysis, TIMI-3 flow was restored in 95.6% of pts, TIMI-2 flow was present in 3.0%, and TIMI-0/1 was present in 1.4%. Mortality at 6 months occurred in 68 pts (3.3%); 2.9% of pts with post procedural TIMI-3 flow died, vs. 6.7% with TIMI-2 flow and 7.1% with TIMI-0/1 flow (p<0.04). TIMI flows and 6 month mortalities by treatment arm appear in the table:

	PTCA	PTCA + Abciximab	Stent	Stent + Abciximab
TIMI-3 flow	95.3%	96.3%	94.6%	96.1%
6 month death	4.3%	2.3%	2.7%	3.8%
6 month cardiac death	4.1%	2.3%	2.3%	3.2%
	All PTCA	**All Stent**	**No Abciximab**	**All Abciximab**
TIMI-3 flow	95.8%	95.4%	95.0%	96.2%
6 month death	3.3%	3.3%	3.5%	3.0%
6 month cardiac death	3.2%	2.8%	3.2%	2.8%

There were no statistically significant differences between any groups. **Conclusions.** Coincident with improved stent technology, post procedural TIMI flow rates are no longer reduced by stent implantation in AMI, and survival is excellent with all mechanical reperfusion strategies in patients without cardiogenic shock.

4:45 p.m.

838-4 **Abciximab Use During Percutaneous Intervention in Patients With Acute Myocardial Infarction Improves Early and Late Clinical Outcomes: Final Results of the CADILLAC Trial**

James E. Tcheng, Mark Effron, Cindy L. Grines, Eulogio Garcia, David Cox, Thomas Stuckey, John Carroll, Giulio Guagliumi, Barry Rutherford, Alexandra J. Lansky, Paolo Esente, John Griffin, Gregg W. Stone. *The Cardiovascular Research Foundation and Lenox Hill Heart and Vascular Institute, New York City, NY, Duke University Medical Center, Durham, NC*

Background. Abciximab (Abx) improves clinical outcomes in pts undergoing elective percutaneous intervention. We hypothesized that the adjunctive use of Abx during primary PTCA and stenting in AMI would improve the early safety profile of the procedure and reduce late adverse events. **Methods.** In the CADILLAC trial, 2082 pts of any age with AMI <12 hrs onset without cardiogenic shock were prospectively randomized in a 2x2 factorial design to primary PTCA or MultiLink stenting, and to Abx or no Abx. The primary endpoint was the 6 month composite occurrence of death, disabling stroke, reinfarction, or ischemia requiring TVR. **Results.** A total of 1,054 pts were assigned to Abx (529 to PTCA and 525 to stent), and 1,028 pts were assigned to no Abx (516 to PTCA and 512 to stent). By core lab analysis, TIMI-3 flow was restored in 96.2% of pts assigned to Abx vs. 95.0% assigned to no Abx (p=0.18). Results by intention to treat appear in the table:

	No Abciximab	Abciximab	P Value
30 day death	23 (2.2%)	19 (1.8%)	0.48
30 day disabling stroke	2 (0.2%)	2 (0.2%)	0.99
30 day reinfarction	6 (0.6%)	7 (0.7%)	0.81
30 day ischemic TVR	43 (4.2%)	25 (2.4%)	0.02
30 day MACE	69 (6.7%)	45 (4.3%)	0.01
30 day severe bleed	4 (0.4%)	6 (0.6%)	0.75
6 month MACE	148 (14.4%)	125 (11.9%)	0.09

The reduction in the 30 day MACE rate with abciximab was more pronounced in pts assigned to PTCA (4.3% vs. 8.1%, relative reduction [RR] 47%, p=0.01) than in those assigned to stenting (4.2% vs. 5.3%, RR 21%, p=NS), as was the reduction in 6 month MACE (14.2% vs. 18.4%, RR 23%, p=0.06, and 9.5% vs. 10.4%, RR 9%, p=NS, respectively.) **Conclusion.** In patients without cardiogenic shock undergoing mechanical reperfusion therapy for AMI, abciximab use during intervention improves early and late clinical outcomes, especially after primary PTCA, without increasing complications.

5:00 p.m.

838-5 **Early Stenting Versus Conservative Treatment After Thrombolysis in Acute Myocardial Infarction**

Bruno Scheller, Benno Hennen, Bernd Hammer, Hans-Peter Stoll, Torsten Markwirth, for the SIAM III study group. *University of Saarland, Internal Medicine III, Homburg / Saar, Germany*

Objectives: Thrombolysis in acute myocardial infarction (AMI) is limited by TIMI III-flow rates of 60% and reocclusion of the infarct related artery. Prior studies showed no benefit of PTCA following thrombolysis compared to thrombolytic therapy alone in AMI. Recent studies, however, have demonstrated superiority of primary stenting versus PTCA alone in AMI. The objective of the SIAM III study (South West German Interventional Study in Acute Myocardial infarction) is to compare the strategy of early coronary stenting (group I) with a conservative treatment (group II) following thrombolysis in AMI. **Methods:** SIAM III is a multicenter, randomized, prospective, controlled study. Inclusion criterion is thrombolysis within 12 hours from the onset of symptoms in AMI. Patients of group I are transferred to the interventional center within 6 hours after thrombolysis for coronary angiography including stenting of the infarct related artery. Group II has elective coronary angiography after two weeks with stenting of the infarct related artery at this time. Primary endpoint is a combined endpoint of death, reinfarction, and target lesion revascularization. **Findings:** So far (august 2000), 166 pts have been randomized. During a mean follow-up time of 159±97 days, early stenting was associated with a significant reduction of the combined end point (22.1% vs 37.7%, p=0.035) of death (5.9% vs 11.6%, ns), reinfarction (2.9% vs 2.9%, ns), and target lesion revascularization (16.2% vs 24.6%, ns). The incidence of ischemic events leading to unplanned rehospitalization or angiography was significantly reduced in group I (2.9% vs 34.8%, p=0.01). Bleeding complications occurred in 10.3% of pts in group I vs 7.2% in group II (ns). TIMI III flow rates at the two week angiography were 98.5% in group I vs 59.0% in group II (p=0.01). Left ventricular ejection fraction two weeks after AMI was 56.7±11.5% in patients undergoing early stenting compared to 52.5±13.4% in the conservative group (p=0.06). **Conclusions:** Early stenting after thrombolysis in AMI is safe. This preliminary data indicate a clinical benefit by this approach compared to conservative treatment after thrombolysis in AMI.

5:15 p.m.

838-6 **Long-Term Survival After Routine Rescue PTCA for Failed Thrombolysis is Similar to That of Successful Thrombolysis**

Philippe G. Steg, Laurent Francois, Bernard Iung, Patrick Charlier, Pierre Aubry, Dominique Himbert, Hakim Benamer, Laurent J. Feldman, Jean-Michel Juliard. *Hôpital Bichat, Paris, France*

Background: Failed thrombolysis is associated with decreased short- and long-term survival. Rescue PTCA has been tested in small clinical trials, but no information is available on the long-term outcome after rescue PTCA for failed thrombolysis. **Methods:** 362 consecutive Pts with acute myocardial infarction receiving lytic therapy for acute infarction were studied. 95% underwent 90 min angiography and 208 (60%) had TIMI 3 flow, 31 (9%) TIMI 2 and 106 (31%) TIMI 0-1 flow. Rescue PTCA was attempted in 91/106 (86%) lytic failures and achieved TIMI 3 flow in 81/91 (89%). Long-term follow-up (up to 10 years) was available in 96% of this cohort. **Results:** 10-year actuarial survival was 81±3%, 85±3% without cardiovascular death, 76±3% without cardiovascular death or infarction, 58±4% without death, infarction or revascularization (event-free survival). Kaplan-Meier analysis shows similar event-free survival among patients in whom TIMI 3 when achieved by lysis alone vs lysis+rescue PTCA (p=0.65). Likewise, survival was similar among patients with successful lytic therapy (TIMI 3 flow) or attempted rescue PTCA (p=0.85). Multivariate analysis of predictors of event-free survival demonstrated that failure of lytic therapy to achieve patency was not a predictor of long-term survival in this cohort with a high rate of rescue PTCA. Conversely, final (i.e. post rescue) TIMI flow, sex, age, number of diseased vessels and left ventricular function were uni- and multivariate predictors of survival and event-free survival.

	Chi-Square	p
Nbr diseased vessels	62.6	<0.0001
LV function	6.4	<0.01
Male gender	8.9	0.003
Interaction TIMI flow-Nbr Diseased vessels	6.1	0.01
Interaction TIMI-LV function	6.2	0.01
TIMI	1.1	0.28

Conclusion: Routine rescue PTCA of patients with failed lytic therapy achieves similar long-term survival to successful lysis for acute myocardial infarction.

ORAL CONTRIBUTIONS

846 New Aspects of Glycoprotein IIb/IIIa Inhibitors in Acute Coronary Syndromes

Tuesday, March 20, 2001, 8:30 a.m.-10:00 a.m.
Orange County Convention Center, Room 230D

8:30 a.m.

846-1 **Immediate Reduction of Microvascular Resistances Following Abciximab Administration in Unstable Angina. Insight Into the Mechanism of Action of GPIIb/IIIa Inhibitors**

Mario Marzilli, Gianmario Sambuceti, Roberto Testa, Silvio Fedele. *Cardio Thoracic Dept, University of Pisa, Pisa, Italy, Institute of Clinical Physiology, CNR, Pisa, Italy*

Background: Platelet glycoprotein IIb/IIIa blockers have been proven to be beneficial in acute ischemic syndromes. Their favourable effects have been attributed to passivation of the active plaque and reduction of the thrombus burden.However, recent studies have shown that benefits from GP IIb/IIIa blockers are independent from the presence of thrombus and from plaque morphology. The purpose of this study was to investigate the mechanism of action of GP IIb/IIIa blockers by simultaneous assessment of their effects on the stenotic coronary segment and the distal coronary vasculature. **Methods:**Nine patients with refractory unstable angina underwent cardiac catheterization and angioplasty. The resistances to flow of the stenotic segment and of the distal coronary vasculature were measured at baseline, during hyperventilation, and during intracoronary adenosine, before and after abciximab administration. Measurements were repeated after PTCA. **Results:** Hyperventilation consistently induced an ischemic attack and increased trans-stenotic (14.9±198.2 mmHg/ml/min vs 6.3±7.0 mmHg/ml/min, p<0.05) and distal (11.2±8.3 mmHg/ml/min vs 8.0±7.2 mmHg/ml/min, p<0.05) coronary resistances to flow. Abciximab had no significant effect on stenosis resistance, while it promptly reduced distal coronary resistance under all study conditions, including baseline (6.0±5.9 mmHg/ml/min, p<0.05), hyperventilation (5.9±5.6 mmHg/ml/min, p<0.01), and adenosine-induced vasodilation (3.7±3.8 mmHg/ml/min vs 5.2±5.4 mmHg/ml/min, p<0.05). Moreover,the hyperventilation test became negative in all patients after abciximab administration, prior to PTCA. **Conclusion:** The observations of this study demonstrate that abciximab administration result in an immediate reduction of coronary microvascular resistance to flow and prevents active coronary vasoconstriction . Improvement of microvascular function may play a prominent role in the beneficial effects of abciximab in acute ischemic syndromes.

8:45 a.m.

846-2 **Optimal Dosing of a Glycoprotein IIb/IIIa Antagonist With a Simplified Renal-Based Algorithm: Pharmacodynamic and Clinical Findings From PARAGON B**

Christopher K. Dyke, Kenneth W. Mahaffey, Lisa G. Berdan, Magnus Ohman, Kristin Newby, Rodney A. Sparapani, Peter B. Berger, Neal S. Kleiman, Harvey D. White, Judith S. Hochman, Frans van de Werf, Paul W. Armstrong, Robert M. Califf, Robert A. Harrington, Eric J. Topol. *Duke Clinical Research Institute, Durham, NC*

Background: PARAGON A and PARAGON B evaluated the glycoprotein IIb/IIIa antagonist lamifiban in patients with non-ST elevation ACS. In a post hoc analysis, PARAGON A demonstrated a relationship between plasma concentration and clinical outcomes. The plasma concentration of lamifiban in a range of 18-42 ng/ml was associated with marked reductions in ischemic outcomes. **Methods:** PARAGON B was designed to prospectively test that a renal-based dosing algorithm could provide an optimal lamifiban concentration that would be associated with an accentuation of small molecule glycoprotein IIb/IIIa benefit. The primary endpoint was a composite of death, MI, or severe recurrent ischemia (SRI). **Results:** Steady state concentrations were reported in 1272 of 2628

patients who received lamifiban. Target concentration was achieved in 919 (72%). Baseline differences associated with a significant likelihood of being out of range included age, sex, and renal insufficiency (CRI). There were no significant statistical differences in the primary endpoint but in a subset of troponin positive patients, an increase in events was seen in the <18 ng/ml group. No statistical differences were seen in bleeding.

	<18 (n=110)	18-42 (n=919)	>42 (n=243)	Placebo (n=2568)
% Total PK Data	8.7	72.2	19.1	NA
Death/MI/SRI (%)	11.9	10.7	9.1	12.8
TnT+ Death/MI/SRI* (%)	19.7	8.7	7.9	19.4
Age>80 (%)	2.7	5.7	9.1	7.2
Female (%)	23.6	33.4	46.1	34.3
CRI (%)	0	0.8	4.5	1.9

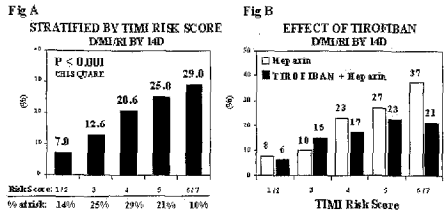
*For lamifiban-treated patients with PK and troponin data. **Conclusions:** Renal-adjustment of the lamifiban infusion rate was successful in achieving target concentration in the majority of patients. However, age>80, female sex, and CRI remained predictors for higher than anticipated serum concentrations despite formula corrections. High-risk patients (troponin positive) with sub-target lamifiban concentrations experienced more frequent adverse ischemic events and had similar outcomes as placebo. These findings highlight the importance of adequate dosing of a glycoprotein IIb/IIIa antagonist.

9:00 a.m.

846-3 An Integrated Clinical Approach to Predicting the Benefit of Tirofiban: Application of the TIMI Risk Score for Unstable Angina/Non-ST Elevation MI in PRISM-PLUS

David A. Morrow, Elliott M. Antman, Carolyn H. McCabe, Eugene Braunwald, Pierre Theroux. *Brigham & Women's Hospital, Boston, MA, Montreal Heart Institute, Montreal, PQ, Canada*

Risk assessment at presentation may guide selection of patients (pts) for whom effective but expensive therapies are most beneficial. The TIMI Risk Score for UA/NSTEMI identifies pts who benefit from treatment with enoxaparin but has not been evaluated for therapy with intravenous GPIIb/IIa inhibitors. **Methods:** The TIMI Risk Score is a simple integer score for predicting the risk of death and recurrent ischemic events based on the sum of 7 clinical characteristics at presentation (age=< 65, >=3 cardiac risk factors, severe anginal symptoms, documented CAD, ST deviation >0.5 mm, elevated cardiac markers, prior ASA use). We evaluated the risk score in 1570 pts with UA/NSTEMI treated with tirofiban + heparin vs. heparin alone in PRISM-PLUS for predicting both the risk of recurrent events and the benefit of tirofiban. In addition, we assessed the prognostic capacity of the 6 remaining variables in pts with negative cardiac markers. **Results:** By 14 days, 288 pts (18.4%) had experienced death, new MI, or refractory ischemia (D/MI/RI). Stratification by the TIMI Risk Score, revealed both a highly significant gradient of increasing risk for D/MI/RI (Fig A), and a strong pattern of increasing benefit of tirofiban with rising risk score ($P_{interact}$ = 0.05, Fig B). Among pts with normal cardiac markers (N=1060), the risk score established a similar 3.5-fold gradient of increasing risk for D/MI/RI (p < 0.001). Further, the risk score (>= 4) identified a population with normal cardiac markers that derived significant benefit from tirofiban (RR 0.73, p = 0.027). **Conclusions:** Applied in pts from PRISM-PLUS the TIMI Risk Score: 1) showed a strong prognostic capacity and revealed an increasing benefit of tirofiban with rising risk score; 2) performed well as a simple clinical tool to aid in the early identification of pts without elevated cardiac markers who should be considered for therapy with more potent antiplatelet therapy.



9:15 a.m.

846-4 Use of the PURSUIT Risk Score Can Provide Accurate Early Risk Stratification in a Nonselected, Community-Based Population With NonST Elevation Acute Myocardial Infarction.

Emmanouil S. Brilakis, Stephen L. Kopecky, Brent A. Williams, Jason Vinar, Ian P. Clements. *Mayo Clinic, Rochester, MN*

Background: In a recent post-hoc analysis of the PURSUIT (Platelet glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin (eptifibatide) Therapy) trial, a risk stratification scheme was proposed. Using 7 clinical parameters [age, gender, worst CCS (Canadian Cardiovascular Society) class in past 2 weeks, heart rate, systolic blood pressure, signs of heart failure, and ST-depression on presenting ECG] a risk score was calculated, which showed strong association with 30-day mortality. However, patients included in the PURSUIT trial had to fulfill specific inclusion criteria. The goal of our study was to examine the predictive accuracy of the PURSUIT risk score in a community-based population with non-ST elevation acute myocardial infarction (AMI).

Methods: The PURSUIT risk score was calculated for 313 consecutive Olmsted County, MN patients presenting to our institution with non-ST elevation AMI between 1988 and 1998. The predicted mortality was then compared with the actual mortality.

Results:

PURSUIT risk score	Number of patients	Estimated 30-day mortality, by PURSUIT risk score (%)	Actual 30-day mortality (%)
0-3	40	0.5	0.0
4-7	66	2.0	0.0
8-11	94	4.5	6.5
12-15	69	8.0	8.7
16-20	44	19.0	20.7

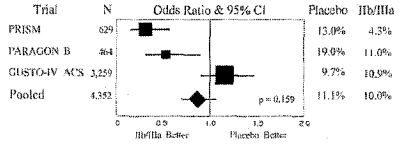
Conclusion: In a community-based population with non-ST segment elevation AMI the PURSUIT risk score allowed an excellent prediction of 30-day mortality. The PURSUIT risk score can be used in non-selected patient populations with non-ST elevation AMI for accurate early risk stratification.

9:30 a.m.

846-5 Striking Heterogeneity of Responsiveness to Glycoprotein IIb/IIIa Inhibition in Patients With Acute Coronary Syndromes and Positive Troponin

Marco Roffi, L. Kristin Newby, Robert A. Harrington, Harvey D. White, Christian W. Hamm, Eric J. Topol. *Cleveland Clinic Foundation, Cleveland, OH*

Background: Previous trials have shown that GP IIb/IIIa are particularly beneficial in the medical management of non-ST elevation acute coronary syndromes (ACS) patients with elevated troponin. However, this benefit could not be reproduced in GUSTO IV ACS. We therefore performed a systematic overview. **Methods:** We included in a meta-analysis the troponin positive populations of the so far performed non-interventional GP IIb/IIIa trials assessing troponin status systematically, namely PRISM (tirofiban for 48 hours), PARAGON B (lamifiban for up to 72 hours), and GUSTO IV ACS (abciximab for 24 or 48 hours). The diagnostic threshold for troponin positivity was troponin-I level of 1.0 µg/L in PRISM, and troponin-T level of 0.1 µg/L in PARAGON B and GUSTO IV ACS. **Results:** As shown in the figure, the incidence of death/MI in troponin positive patients was highly significantly reduced by GP IIb/IIIa inhibitors in PRISM and PARAGON B (p<0.001 and p<0.016, respectively) but not in GUSTO IV ACS (p=0.26). Driven by the latter trial, the meta-analysis showed no overall benefit (p=0.16). The impact of GP IIb/IIIa blockade was strikingly heterogenous across the trials (as documented by Breslow-Day test p<0.001). Unlike the previous trials, in GUSTO IV ACS troponin positivity was per se an inclusion criteria. This led to a different patient population enrollment with a clearcut lower event rate (9.7 vs. 13-19 % in the placebo group), less responsive to GP IIb/IIIa inhibition. Alternatively or additionally, the different benefits may be due to variable drug action.



Conclusions: The data in aggregate demonstrate substantial heterogeneity in troponin positive ACS patients for response to IIb/IIIa blockade. Troponin responsiveness to IIb/IIIa blockade has only been validated by retrospective assessment in ACS trials; further trials prospectively assessing the value of troponin in ACS are warranted.

9:45 a.m.

846-6 Reversibility of Platelet Inhibition Associated With Small Molecule, Competitive GPIIb/IIIa Antagonists: An In Vitro Model for Clinical Management Strategies

Richard C. Becker, You Fu Li, Frederick A. Spencer. *University of Massachusetts Medical School, Worcester, MA*

Background: Platelet surface glycoprotein (GP) IIb/IIIa (µ IIb/b_3) receptor inhibition, by preventing fibrinogen binding, attenuates hemostatic potential. Because small molecule antagonists have relatively low GPIIb/IIIa receptor affinity (and high circulating plasma concentrations), it has been assumed that: 1)platelet transfusions would not effectively restore physiologic aggregability, and 2) alternative substrates would be required to manage hemorrhage events. **Methods:** Washed platelets from 24 healthy volunteers were suspended in tyrodes buffer and incubated with steady state concentrations (in vivo) of tirofiban or eptifibatide prior to activation with TRAP (15µM). In a separate series of experiments, platelet inhibition >90% (in response to 5µM ADP) was achieved with tirofiban or eptifibatide. Recovery of platelet aggregation was determined following fibrinogen and/or platelet supplementation. **Results:** Platelet inhibition was reversed by the addition of fibrinogen in a concentration-dependent manner. Recovery of platelet aggregability toward a physiologic level was achieved with fibrinogen (0.76-0.80 g/L), platelets (2.4×10^{11}/L) or their combination. The findings are summarized below:

Recovery of Platelet Aggregation (%)

Treatment	FgN (0.75 g/L) (A)	Plt. 1 (1.2×10^{11}/L) (B)	FgN + Plt. (C)	Plt. 2 2.4×10^{11}/L) (D)	FgN + Plt. 2 (E)
Mean +/- SD	30.8 ± 12.4	28.9 +/- 10.5	40.5 +/- 11.0	54.4 +/- 12.9	67.3 +/- 12.1
(A) vs -		P=0.69	P<0.05	P<0.00003	P<0.0001
(B) vs -			P<0.05	P<0.0001	P<0.0001
(C) vs -				P<0.05	P<0.0001
(D) vs -					P<0.05

Conclusions: Effective reversibility of small molecule, competitive GPIIb/IIIa antagonists and restoration of platelet-mediated hemostatic potential can be achieved with either fibrinogen supplementation (equivalent of 8 units fresh frozen plasma) or platelet transfusion (equivalent of 8 units pooled platelets). Combined administration should be considered in the setting of life-threatening hemorrhage or when hemostasis is comprised in association with major surgery.

POSTER SESSION

1182 Coronary Bypass Operation Without Extracorporeal Circulation

Tuesday, March 20, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 10:00 a.m.-11:00 a.m.

1182-79 Beating Heart Versus Conventional Coronary Artery Bypass: Early Versus Late Postoperative Neurological Complications

Garrett K. Peel, Sotiris C. Stamou, Peter C. Hill, Ammar S. Bafi, Mercedes K. C. Dullum, Albert J. Pfister, Steven W. Boyce, Jorge M. Garcia, Paul J. Corso. *Washington Hospital Center, Washington, DC*

Background: Coronary artery bypass grafting without cardiopulmonary bypass (Off-pump CABG) has been associated with comparable or lower rates of postoperative neurological complications compared to the conventional approach (On-pump CABG). It is unknown, however whether the timing of occurrence of neurological complications is different between these two approaches. **Methods:** New neurological complications were considered as a single end point and were categorized with respect to whether they were detected within the first 2 days after surgery (early) or more than 3 days, after an initial, uneventful neurological recovery from surgery (delayed). We compared the occurrence of early and delayed neurological complications after On-pump (n=3980) Vs. Off-pump CABG (n=1563) between January 1998 and July 2000. The two groups were similar with respect to baseline characteristics and risk stratification; the Northern New England cardiovascular disease study group estimated risk of cerebrovascular accident was 1.9% for both groups. **Results:** The rate of neurological complications was 4.9 % (n=194) for the On-pump group Vs. 2.7 % (n=42) for the Off-pump group and stroke rate was 2.3% (n=93) Vs. 1.3% (n=21), respectively. Of patients who had neurologic complications the incidence of early or delayed events between on and off-pump CABG is summarized in table (all analyses were significant at the level of p<0.001). **Conclusions:** Among patients experiencing neurological complications after surgery, Off-pump CABG patients are at a lower risk of immediate but are at a higher risk of late postoperative neurological complications than On-pump CABG. Different mechanisms may be implicated in the pathogenesis of neurological adverse events between the two approaches.

	On-pump (n=194)		Off-pump (n=42)	
	Early	Delayed	Early	Delayed
All Neurological complications	118 (61%)	76 (39%)	6 (14%)	36 (86%)
Stroke (deficit> 72 hours)	52 (56%)	41 (44%)	3 (14%)	18 (86%)

1182-80 A Large Unselected Series of Consecutive OPCAB Patients Demonstrates Reduced Hospital Morbidity and Mortality

Mark W. Connolly, Valavanur A. Subramanian, Nilesh U. Patel, John C. McCabe, Mark H. Genovesi, Didier F. Loulmet, Rita M. Considine, Archana Maini. *Lenox Hill Hospital, New York, NY*

Objective: To assess the potential benefits of multivessel CABG without cardiopulmonary bypass (OPCAB), a committed, intention-to-treat OPCAB program was begun for all patients requiring multivesssel primary CABG. **Methods:** In a retrospective analysis 430 unselected, consecutive OPCAB patients (July 1999-July 2000) were compared to 453 conventional CABG patients (July 1997-July 1998). The OPCAB patients were significantly older (66.7 yrs. vs. 64.5 yrs.) and had a higher incidence of more than one previous MI (10% vs 6%), diabetes mellitus (39% vs 34%), HTN (77% vs 70%), CHF (81% vs 45%), and renal failure (8.4% vs 2.6%). The mean number of grafts performed was less in OPCAB (3.2 + 0.9 vs 3.4 + 0.9, p< 0.0001). Conversion to CPB occurred in 11 patients (2.6%, one death). **Results:** Compared to conventional CABG, OPCAB including CPB conversion patients had a significantly less overall complication rate (45/430, 11% vs 86/453, 19%, p<0.001), deep sternal infection (5/430, 2.3% vs 16/453, 5.3%, p<0.03), reop for bleeding (10/430, 1.2% vs 24/453, 3.5%, p<0.02), percentage of patients transfused (50% vs 67%, p<0.0001), mean number of PRBC's units transfused per patient (3.1 + 3.2 vs 1.8 + 5.5, p<0.0002), and operative mortality (8/430, 1.9% vs 20/453, 4.4%, p<0.03). Approaching significance (p<0.07), OPCAB had a lower stroke rate of 1.4% (6/430) compared to 3.1% (14/453) for CABG. As OPCAB had a higher risk profile, risk-adjusted operative mortality (NYSCSRS) was 1.3% compared to 3.9% for CABG. Multi-regression analysis demonstrated age, ejection fraction, calcified aorta, and conventional CABG as significant factors for operative mortality (p<0.0001). Length of stay was also less in OPCAB (6.1 days vs 7.5 days, p<0.0001). **Conclusion:** Even including conversion to CBP patients, this large, retrospective series of consecutive, unselected OPCAB patients achieved significantly lower hospital complications and mortality compared to conventional CABG. Methods to prevent conversion to CPB may further improve results.

1182-81 Off-Pump Versus On-Pump CABG Surgery: Determinants and Surgical Outcomes Among 51 Surgeons Doing Both Procedures

Michael J. Mack, April W. Simon, Edmund R. Becker, Steven D. Culler, Lynn G. Tarkington, Salvatore Battaglia, Michael P. Macris, Sameer Mehta. *Medical City Dallas, Dallas, TX, Emory University Rollins School of Public Health, Atlanta, GA*

Background: The growth in off-pump CABG (OPCAB) raises questions about when it is appropriate versus an on-pump (OnP) approach. Of those surgeons who use both OPCAB and OnP techniques, what factors influence their decision? We compare surgeons who perform both OPCAB and OnP surgery to evaluate differences in patient characteristics and surgical outcomes. **Methods:** The 1999 HCA Case Mix Database contains data from 75 facilities and 17,609 CABG surgeries (DRGs 106, 107, and 109). For surgeons who performed 10 or more OPCAB and 10 or more OnP surgeries in 1999, we compared their OPCAB and OnP performance for 19 patient characteristics and 14 surgical outcomes. **Results:** The 51 surgeons performed 5,508 CABGs, an average of 30 OPCAB and 78 surgeries OnP. OnP use increased for surgeons as the number of bypassed vessels increased (see table). Patients with preop AMI were significantly more likely to be OnP and OnP patients were more likely to have neurological complications. For these surgeons, death rates OnP were more than double their OPCAB rates. Of the remaining 33 variables analyzed, none were statistically significant (p=0.05). However, acute renal failure and percentage of patients discharged directly home without further structured medical support were trending toward significance. **Conclusion:** For surgeons performing both OPCAB and OnP, there are significant differences in both mortality and neurologic complications. Given these results, further research is needed to determine which patients are best suited for this surgical approach.

	OPCAB	OnP	p Value
# of Bypass Vessels	2.51	3.43	<0.001
PreOp AMI	23.12%	25.60%	0.036
Acute Renal Failure	2.72%	4.05%	0.071
Neuro Complications	0.66%	1.81%	0.031
Discharge Home	87%	84%	0.065
Mortality	1.39%	3.06%	0.001

1182-82 Outcome in Patients Undergoing Redo CABG With and Without Cardiopulmonary Bypass

Martin Czerny, Daniel Zimpfer, Vedat Sahin, Harald Baumer, Juliane Kilo, Andreas Zuckermann, Ernst Wolner, Michael Grimm. *Department of Cardiothoracic Surgery-University of Vienna, Vienna, Austria*

Background: The aim of this study was to compare morbidity, mortality and functional status after redo coronary artery bypass grafting (CABG) with and without cardiopulmonary bypass in a retrospective study design. **Methods:** We compared morbidity, mortality and functional status in 53 elective patients having undergone redo CABG between January 1998 and April 2000. Twenty-four patients underwent redo CABG with and 29 patients underwent redo CABG without CPB. Mean EURO score was 7.5+/-0.7 in patients with and 7.0+/-0.6 in patients undergoing CABG without CPB (ns). Parsonnet score was 15.4+/-1.2 and 15.0+/-1.4, respectively. Follow-up was defined by means of survival, freedom from recurrence of angina (Canadian Cardiovascular Society Score), freedom from rehospitalisations and reinterventions as well as need for antianginal medication. Patient follow-up was performed either by telephone or a mailed questionnaire. Follow-up was complete in all patients. **Results:** There were 3 perioperative deaths in the group with CPB and 1 perioperative death in the group without CPB (ns). Those 4 patients who died, had a significantly higher EURO score than the survivors- EURO score 10.3+/-0.5 vs 7.0+/-3.3 (P=.0001), Parsonnet score 18.8+/-6.7 vs 14.9+/-6.7 (ns). In the group of patients operated with CPB, 83% of patients received complete revascularization. In the group without CPB, 14% received complete revascularization (P=.00001). The mean follow-up period in patients with CPB was 19 months and 14 months in patients without CPB (ns). During follow-up, death was not observed. At the time of follow-up, mean CCS score in patients having undergone redo CABG with CPB was 1.4+/-0.8 and in patients without CPB 1.6+/-0.8 (ns). Patients after redo CABG without CPB had a higher use of nitrates at follow-up (P=.013). **Conclusions:** Myocardial revascularization without cardiopulmonary bypass may represent a safe and effective therapeutic modality for patients requiring redo CABG, resulting in lower hospital morbidity and mortality. Despite the lower number of bypass grafts and the higher use of nitrates in patients without CPB, medium-term outcome is well comparable to patients having undergone redo CABG with CPB.

1182-83 Minimally Invasive Direct Coronary Artery Bypass Versus Off-Pump Coronary Artery Bypass: A Study in Clinical Appropriateness in 226 Patients

Kevin A. Richardson, Robert E. Michler, Randall K. Wolf, David A. Brown. *Ohio State University Medical Center, Columbus, OH*

Background: Coronary artery bypass without the aid of extracorporeal circulatory support is gaining popularity as an alternative to conventional on-pump techniques. These techniques include minimally invasive direct coronary artery bypass (MIDCAB) and median sternotomy, off-pump coronary artery bypass (OPCAB). This study evaluated these two surgical methods and compared clinical outcomes for patients with single vessel left anterior descending artery (LAD) disease.

Methods: Outcomes were analyzed for patients with LAD disease who underwent MIDCAB (n=156) vs OPCAB (n=70) between January 1, 1997 and June 30, 2000. These groups were similar in risk stratification and patient characteristics. Data was collected prospectively and analyzed using Chi-Square and Fisher Exact tests.

Results: During this time period, 1537 bypass procedures were performed, 303 were done without cardiopulmonary bypass. Of these, 226 were performed for isolated LAD disease. The incidences of postoperative complications for MIDCAB vs. OPCAB were as follows: reoperation rate, 1.92% vs 1.43% (p=0.09); graft occlusion, 2.56% vs 0 (p=0.33); myocardial infarction, 0.64% vs 0 (p=0.17); atrial fibrillation, 3.21% vs 4.29% (p=0.08); infection, 1.28% vs 0 (p=0.03); neurologic events, 0.64% vs 2.86% (p=0.22); renal failure, 0.64% vs 1.43% (p=0.09); prolonged ventilation 0 vs 1.43% (p=0.17); chronic pain syndrome, 3.21% vs 0 (0.29); mortality, 0.64% vs 2.86% (p=0.09). The postoperative length of stay for the MIDCAB vs OPCAB groups was 3.91 +/- 3.34 days vs 4.45 +/- 2.24 days.
Conclusion: Our experience with minimally invasive surgery shows there is no clinically significant difference between MIDCAB and OPCAB approaches. Although some have claimed an advantage with the MIDCAB technique with respect to patient recovery and cosmetics, our raw data would suggests a trend toward less morbidity with the OPCAB method. Prospective randomized trials will further delineate this issue.

POSTER SESSION

1183 Myocardial Preservation: Mechanistic Insights

Tuesday, March 20, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 10:00 a.m.-11:00 a.m.

1183-84 Protective Effects of Adenosine on Myocardial Ischemia and Reperfusion in the Dogs

Hela Aschour, Ali Denktas, Abid Assali, James Amirian, Patty Felli, Maximilan Buja, Margaret Uthman, Richard W. Smalling. *University of Texas Medical School, Houston, TX*

Background: Although intracoronary adenosine has been shown to improve angiographic evidence of coronary blood flow post reperfusion in humans, its physiologic and mechanism of action is unknown at the present time.
Objective: To evaluate the effect of intracoronary adenosine bolus prior to reperfusion and its effect on white blood cell (WBC) activation, Icam-1 expression, end diastolic wall thickness (EDWT) and infarct size.
Methods: Fourteen open chest dogs were subjected to two hour occlusion of mid-left anterior descending (LAD) artery followed by four hours of reperfusion.
The dogs were instrumented with sonomicrometer crystals to measure EDWT in the LAD artery and circumflex (CX) regions. Hemodynamic measurements were done at baseline, ten minutes after occlusion, and then at one hour intervals until the end of the experiment. Twenty-four micrograms of adenosine were injected over two minutes distal to the cuff occluder just prior to reperfusion in the treated animals and an equal volume of saline in the control animals.
The findings were compared using analysis of variance.
Results: Ten minutes after reperfusion, there was an abrupt increase in the EDWT in both control and adenosine groups that is a sign of irreversible reperfusion injury. The Icam-1 measurements by immunohistochemistry were significantly higher in the control group compared to the adenosine group (P=0.0001). Myeloperoxidase production (WBC activation) was reduced significantly in the infarct and ischemic regions with the adenosine compared to saline(P<0.05,P<0.01 respectively). A trend towards a reduction in infarct size was noted when expressed as a percentage of the area at risk (control 48.04%±9.24%, adenosine 58.20%±13.37%,P<0.07).
Conclusions: In this study, we demonstrated that 24ug of intracoronary adenosine injection prior to reperfusion provides an intermediate benefit in infarct size reduction compared to saline administration. This can be due in part to a suppresion of neutrophil activation and adhesion (reperfusion injury) to endothelial cells.

1183-85 Protective Effect of Increased Glycolysis in Chronically Infarcted Hearts

Franz R. Eberli, Regina Berchtold, Gert Printzen, Thomas Schaffner, Bernhard Meier. *Swiss Cardiovascular Center Bern, Bern, Switzerland*

Background: Following a myocardial infarction (MI) hearts increase their capability to generate energy via the glycolytic pathway in the non-infarcted myocardium. We hypothesized that this metabolic remodeling might convey an increased tolerance towards a subsequent ischemia-reperfusion injury.
Methods: 8 weeks after Sham operation or experimental infarction isolated, blood perfused rat hearts were exposed to 30 min of ischemia (10% of initial flow) and 30 min of reperfusion. Hearts with intact glycolysis and normal substrates (glucose, lactate, palmitate) (Sham-Control [n=10] and MI-Control [n=10]) were compared to hearts with blocked glycolysis (Sham–Glyc [n=11] and MI-Glyc [n=7]). Glycolysis was blocked by infusing 100 µM iodoacetate over 15 min after pretreatment with glucagon during glucose free perfusion.
Results: Infarct size in MI-Control vs. MI-Glyc was similar (30±3% vs 28±3% of LV; ns). MI-Control hearts exhibited less ischemic diastolic dysfunction than Sham-Control hearts (LVEDP at end ischemia 30±5 vs. 46±7 mmHg; p<0.05). In contrast, when glycolysis was blocked, ischemic diastolic dysfunction was increased in MI-Glyc compared to MI-Control (p<0.05) and similar to Sham-Glyc (52±3 vs. 54±5 mmHg; ns). Recovery of LV developed pressure was similar in Sham-Control vs. MI-Control (73±4% vs 77±2%; ns), and reduced to similar level in Sham-Glyc and MI-Glyc (52±3% vs. 42±9%; ns). The improved tolerance towards ischemia of MI-Control hearts could not be explained by differences in residual coronary flow and oxygen consumption. However, glycolytic flux, as indexed by total lactate production was increased in MI-Control vs. Sham-Control (28±5 vs. 16±3 mm/gLV; p<0.05). After blockade of glycolysis lactate production was almost absent and identical between Sham-Glyc and MI-Glyc (2±1 vs. 2±1; ns).
Conclusion: Chronically infarcted hearts exhibit an increased tolerance towards subsequent ischemic injury compared to normal hearts. Our results suggest that increased glycolytic activity in the non-infarcted myocardium contributes to the improved ischemic tolerance of chronically infarcted hearts.

1183-86 Cyclosporin A Inhibits Cytochrome c Release and Prevents Myocardial Cell Death Induced by Ischemia/Reperfusion

Zhe Jiao, Olena M. Gorodnya, Xi-Ming Yang, Tai-Hwang M. Fan. *University of South Alabama, Mobile, AL*

Background: The mitochondrial permeability transition pore (MPTP) plays a pivotal role in both apoptosis and necrosis. Persistent MPTP opening causes swelling and uncoupling of mitochondria and results in necrosis. Transient MPTP opening may lead to apoptosis via release of cytochrome c. The present study examined whether cyclosporin A (CsA), a calcineurin inhibitor and a potent MPTP inhibitor, could attenuate the release of cytochrome c and prevent myocardial cell death induced by ischemia/reperfusion. Additionally, we tested whether FK506, another immunosuppressive drug that acts via calcineurin inhibition while having no effect on the MPTP, could also protect the heart.
Methods: Adult rabbit hearts perfused in the Langendorff fashion were subjected to 30 min of global ischemia followed by 2 h of reperfusion. CsA or FK506 were given as a 15-min infusion prior to the onset of global ischemia. Infarct size was determined by computer morphometry of TTC stained sections. Cytosolic cytochrome c levels were determined by Western blot analysis in a separate series of hearts, in which serial biopsies were taken at baseline and at 5, 10, 20, 30, 60, 90, 120 min of ischemia. **Results:** Compared to the control group, the CsA and FK506 groups demonstrated significantly better preserved contractile function following reperfusion. The infarct size was significantly smaller in the CsA group (7±1%, n=6) as compared to the control group (50±5%, n=6) and the FK506 group (19±5%, n=8). In the control hearts, ischemia caused a progressive rise in the cytosolic cytochrome c levels during the initial 30 min of ischemia, reaching a peak of 4.5-fold the pre-ischemic level. CsA completely abolished the rise in cytosolic cytochrome c levels. In contrast, FK506 had little effect on cytochrome c release induced by ischemia. **Conclusion:** The calcineurin inhibitors CsA and FK506 are excellent cardioprotective agents against ischemia/reperfusion injury. The apparent superiority of CsA over FK506 may be attributable to the unique inhibitory action of CsA on the MPTP. Drugs that interfere with cytochrome c release may be good targets for screening for clinically useful anti-infarct agents.

1183-87 Cardioprotection by an Adenosine A2A Receptor Agonist in a Canine Model of Myocardial Stunning Produced by Multiple Episodes of Transient Ischemia

David K. Glover, Mirta Ruiz, Kazuya Takehana, Frank D. Petruzella, Jayson M. Rieger, Timothy L. Macdonald, Denny D. Watson, Joel Linden, George A. Beller. *University of Virginia, Charlottesville, VA*

Background: Stimulation of adenosine A_{2A} receptors on inflammatory cells is inhibitory. We hypothesized that infusion of a highly potent and selective adenosine A_{2A} agonist, ATL146e, would inhibit post-ischemic cardiac inflammation and therefore improve left ventricular (LV) function in a canine model of myocardial stunning.
Methods: Accordingly, 22 open-chest dogs underwent either 4 or 10 cycles of 5 minute left anterior descending coronary artery (LAD) occlusions (OCC) interspersed by 5 or 10 minutes of reperfusion (REP). Left ventricular thickening was measured with ultrasonic crystals beginning at baseline and continuing for 180 minutes after the last occlusion/reperfusion cycle. Regional flow was measured with microspheres. In 11 of the 22 dogs, ATL-146e was infused i.v. prior to occlusion #1 and continued throughout reperfusion at a dose below that which produces vasodilatation (0.01 µg/kg/min).
Results: Myocardial flow was similar between control and ATL-146e treated animals at all times, confirming the absence of vasodilatation. During occlusion, there was severe dyskinesis with marked LAD zone thinning in all animals. As shown in the table, there was significantly greater recovery of LAD zone thickening after reperfusion with ATL-146e in both the 4 (56% vs 91%)and 10 cycle (-5% vs 59%) occlusion-reperfusion groups.

Recovery of LAD Zone LV Thickening During Reperfusion (% Baseline)

OCC-REP	Treatment	# Dogs	5 min REP	180 min REP
4 cycles[1]	Control	6	35±8†	56±12†
4 cycles[1]	ATL-146e	6	57±9†	91±7†*
10 cycles[2]	Control	5	6±12†	-5±11†
10 cycles[2]	ATL-146e	5	47±10†*	59±8†*

† $p < 0.01$ vs Baseline; * $p < 0.05$ Control vs ATL-146e.

Notes:[1] OCC=5 min;REP=10 min [2] OCC=5 min;REP=5 min
Conclusion: The striking amount of functional recovery observed with ATL-146e supports its further evaluation for the attenuation of post-ischemic stunning after reperfusion therapy in patients.

1183-88 Pretreatment With Delta-Opioid Receptor Blockade Attenuates the Reduction of Apoptosis Associated With Ischemic Preconditioning or Morphine-Induced Cardioprotection in Rabbit Ischemia/Reperfusion Model

Shinji Okubo, Yujirou Tanabe, Nakaba Fujioka, Noboru Takekoshi, Rakesh C. Kukreja. *Kanazawa Medical University, Uchinada, Japan*

We have proposed that myocardial protection associated with ischemic preconditioning(IPC) in rabbit hearts involved in the delta-opioid receptor. We examined whetherIPC attenuates irreversible ischemic reperfusion injury in part by decreasing apoptosis and whether the delta-opioid receptor can regulate the apoptosis formation in cardioprotection. Six groups of rabbits were studied . All rabbits underwent sustained coronary artery occlusion(CAO) for 30 min followed by 180 min of reperfusion. IPC was elicited with 4 cycles of 5 min regional ischemia plus 10 min reperfusion before sustained CAO. 1)Control(C)(n=8), 2)IPC(n=8), 3)Morphine (treatment with 3 mg/kg, iv, 15 min before sustained ischemia)(Mor) (n=8), 4)Naloxone(treatment with 10 mg/kg, iv, 10 min before IPC)(Nal+IPC) (n=8). To determine if the delta-opioid receptor has a role in IPC and morphine-induced cardioprotection, naltrindole(NTI), a selective delta-opioid receptor antagonist was utilized; 5)NTI(treatment with 10 mg/kg, iv, 10 min before IPC)(NTI+IPC) (n=8), and 6)NTI(10 mg/kg, iv)+Mor(3 mg/kg, iv) were given 15 min before sustained CAO(n=8). Infarct size(infarct size as a percent of the area at risk) was significantly($p<0.01$) reduced in preconditioned and Mor treated group compared with control, Nal+IPC, NTI+IPC and NTI+Mor group (C:46% vs PC:12% vs Mor:15.3% vs Nal+IPC:48.5% vs NTI+IPC:44.5% vs NTI+Mor:49.3%). The percentage of Apop Tag-labeled cells(DNA fragmentation) was determined with a microscope containing an eyepiece grid(x200 magnification).The percentage of apoptotic cells was calculated for the ischemic region. The findings of DNA fragmentation were significantly($p<0.01$) decreased in ischemic preconditioned group and Mor treated group compared with control, Nal+IPC, NTI+IPC and NTI+Mor group (C:22% vs PC:7.2% vs Mor:10.2% vs Nal+IPC:18.5% vs NTI+IPC:20.3% vs NTI+Mor:19%). This study suggests that IPC reduces lethal ischemic injury in part by decreasing apoptosis(DNA fragmentation) after ischemia/reperfusion and activation of the delta-opioid receptor may play a crucial role in IPC or morphine-induced myocardial protection in the rabbit.

1183-89 Intravenous Use of Dimethylsulfoxide to Improve Outcome of Acute Myocardial Ischemia in a Porcine Model

Dennis W. Dunning, George Eyster, Kevin L. Kelco, Echo Hansen, Earl T. Hawkins, Shirley Siew, Lynn Cronin, William W. O'Neill. *William Beaumont Hospital, Royal Oak, MI, Michigan State University - College of Veterinary Medicine, East Lansing, MI*

Background: Relief of ischemia by tissue reperfusion is the mainstay of therapy to reduce necrosis in an acute myocardial infarct (AMI). Blood and O2 returning to injured tissue can lead to further cellular damage and lethal arrhythmias. We hypothesized that treatment with dimethylsulfoxide (DMSO), an antioxidant, anti-inflammatory, and membrane stabilizer, would improve outcome in AMI. **Methods:** We caused myocardial ischemia in 3 groups of pigs by 30-minute inflation of an intra-coronary balloon in the distal LAD. One group served as controls and 2 treatment groups received intravenous (IV) DMSO as a pre-treatment (early group) or 15 minutes after the start of balloon inflation (late group). ECG and arterial BP were monitored during the procedure. Two-D echocardiograms were done before the cath and <30 minutes after balloon deflation. After 48 hours the hearts were harvested and stained with triphenyl tetrazolium chloride (TTC) to determine areas of necrosis and myocardium at risk. Routine H&E staining was done. **Results:** The pre-treatment group had less necrosis (8.3% +/- 6.7), as a percentage of area at risk, compared to controls (24.3% +/- 10.2, P= 0.0367). The late group (30.6% +/- 9.1) was not significantly different from controls. Histology validated TTC staining. The combined end-point of VF or VT during reperfusion was higher in controls (77.8%) vs either treatment group (early 28% and late 0%, P=0.018). Further analysis showed the difference to be most significant in the late group (P=0.021). ST segment change in the early group was less vs controls (2 mm vs 4.22 mm, P=0.043). Wall motion index was increased similarly in early and control groups, but less in the late group (P=0.023). Blood pressure did not decrease with DMSO. **Conclusions:** IV DMSO may be useful in limiting myocardial necrosis and arrhythmia's during tissue reperfusion. The potection against cell death is greatest when given as a pre-treatment before the onset of ischemia, but benefits extend to late treatment as well.

1183-90 Diazoxide Preserves Oxidative Phosphorylation and the Structural Integrity of Cardiac Mitochondria From Anoxic Injury

Cevher Ozcan, Ekhson L Holmuhamedov, Arshad Jahangir, Andre Terzic. *Mayo Clinic, Rochester, MN*

Background: Myocardial energetics, which primarily rely on oxidative phosphorylation, are highly vulnerable to anoxia. Mitochondrial ATP-sensitive potassium channel (mito-KATP) openers have emerged as powerful cardioprotective agents, yet direct evidence demonstrating the ability of mito-KATP openers to preserve mitochondria against anoxic injury is lacking. **Methods:** Mitochondria were isolated from rat hearts, subjected to 20 min anoxia followed by reoxygenation, and mitochondrial function and structure assessed using selective-minielectrodes, fluorometry, HPLC, and electron microscopy. **Results:** in the absence of a potassium channel opener, anoxia/ reoxygenation decreased the rate of ADP-stimulated oxygen consumption, inhibited ATP production and disrupted mitochondrial membrane integrity. On average, anoxia inhibited ADP-stimulated respiration from 291+/-14 to 141+/-15 ng-atoms O2/min/mg pritein and decreased the rate of ATP production from 752+/-14 to 414+/-34 nmoles ATP/min/mg protein. Following anoxia, the majority (88%) of mitochondria were damaged or swollen with only 12% remaining intact. Diazoxide (100uM), added prior to anoxia, maintained ADP-stimulated respiration at 255+/-7 ng-atoms O2/min/mg protein and ATP production at 640+/-39 nmoles ATP/min/mg protein. Diazoxide also preserved mitochondrial structure, so that following anoxia 67% of mitochondria remained with an intact morphology and adenylate kinase confined to the mitochondria. **Conclusion:** The present study demonstrates that diazoxide prevents anoxia- induced functional and structural deterioration of isolated cardiac mitochondria. By directly protecting mitochondria, the prototype mito-KATP channel opener could maintain myocardial energetics under conditions of reduced oxygen availability, with possible implications in myopreservation.

POSTER SESSION

1184 Stabile Ischemic Syndrome: Stress Testing and Risk Stratification

Tuesday, March 20, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 10:00 a.m.-11:00 a.m.

1184-91 Right Ventricular Performance Is Preserved During Stress in Patients With Chronic Proximal Right Coronary Occlusion

Soo-Teik Lim, Pamela Marcovitz, William W. O'Neill, James A. Goldstein. *William Beaumont Hospital, Royal Oak, MI*

Introduction: In patients with proximal right coronary artery (RCA) occlusion and right ventricular (RV) infarction, resting RV performance typically improves over time, even without reperfusion. However, whether exercise RV performance during stress is preserved in patients with chronic total proximal right coronary artery (RCA) occlusion is unknown. **Methods:** In 20 patients with angiographically documented chronic proximal RCA occlusion, RV free wall (FW) wall motion (1=normal, 2=hypokinetic, 3=akinetic, 4=dyskinetic) was analyzed at rest and peak exercise during stress echocardiography. Angiograms were analyzed for the location of total occlusion relative to the RV branches, as well as the presence of collaterals. **Results:** The RCA was 100% occluded proximal to the RV branches in all cases. Prominent collaterals to the occluded RCA were noted in 19/20 (95%) patients. Resting RVFW motion was normal in 16/20 (80%) pts, whereas mild abnormalities were present in 4 others. For the entire group, RVFW motion was intact (RVFW motion score = 1.13+/-0.31). At peak stress, RVFW motion increased appropriately in 18/20 (90%) of cases, including all 4 pts with resting RVFW abnormalities. However, 2 (10%) patients with normal resting RVFW motion developed exercise induced wall motion abnormalities. Nevertheless, for the entire group, overall RVFW motion score improved during stress (rest=1.13+/-0.31 to 1.06+/-0.18, $p<0.05$). **Conclusion:** In patients with chronic proximal RCA occlusion, RV free wall performance is typically maintained at rest and responds physiologically to stress, undoubtedly reflecting the beneficial effect of collaterals. The few patients in whom RVFW contraction abnormalities developed during exercise likely reflect collateral insufficiency. Given the importance of RV performance under conditions of severe LV dysfunction, these findings may have implications for patients with chronic multivessel ischemic heart disease and severe ischemic cardiomyopathy.

1184-92 Exercise Thallium-201 Myocardial Image Is Useful for Predicting Adverse Outcomes in Patients With Vasospastic Angina

Akihiro Nakagomi, Satoshi Aoki, Yoshito Yamane, Takeshi Yamamoto, Nobuhiko Fujita, Chikao Ibuki, Yoshiki Kusama, Morimasa Takayama, Kouichi Nagasawa, Teruo Takano. *Nippon Medical School, Tokyo, Japan, Tama-Nagayama Hospital, Nippon Medical School, Tokyo, Japan*

The usefulness of exercise thallium-201 myocardial image (ETM) for predicting adverse outcomes in patients (pts) with vasospastic angina (VSA) was examined. Ninety pts with VSA were enrolled in this study. VSA was defined as typical chest pain at rest and on exertion and positive for intracoronary acetylcholine provocation testing and normal coronary angiogram (<25% luminal stenosis) after the intracranary administration of nitroglycerin (NTG). Multiple factors including ETM findings, clinical characteristics, blood chemical variables and coronary flow reserve (CFR) using a Doppler flowwire were analyzed in a prospective study fashion. Seventeen segments of the left ventricle were semi-qualitatively scored on ETM study on a scale ranging from 0 (normal) to 4 (absent) uptake, and the sum of each segment was defined as defect score (DS). Seventy-three patients were stabilized by Ca antagonist and/or nicorandil, however, 17 patients did not respond to these medications and need sublingual NTG during anginal attacks and 2 patients suddenly died probably due to fatal arrhythmia. The relation between DS, clinical characteristics, blood chemical variables, CFR and adverse outcomes (refractory to anti-anginal therapy and death) was analyzed using univariate and multiple logistic regression analysis. Univariate analysis indicated that white cell count ($p=0.01$), plasma fibrinogen level ($p<0.01$) at presenatation, delta BS (30 minutes blood sugar value-fasting blood sugar value, $p=0.02$) and delta IRI (30 minutes insulin value- fasting insulin value, $p=0.04$) during 75g of glucose tolerance test, CFR ($p<0.01$) and DS ($p<0.001$) were associated with adverse outcomes. However, the only variable independently associated with adverse outcomes in multivariate analysis was DS ($p=0.01$). These data indicated that ETM is useful for selecting therapeutic strategy and predicting adverse outcomes in patients with vasospastic angina.

1184-93 Electromechanical Left Ventricular Mapping With Dobutamine Stress for Detection of Myocardial Viability

Khaled R. A. Nour, Julian P. J. Halcox, Shmuel Fuchs, Vandana Sachdev, Julio A. Panza, Vasken Dilsizian, Rita Mincemoyer, Ran Kornowski, Arshed A. Quyyumi. *Cardiology Branch, National Institutes of Health, Bethesda, MD, Washington Hospital Center, Washington, DC*

Background:NOGA left ventricular (LV) electro mechanical mapping (EM) has been used to detect viability in hypoperfused dysfunctional myocardial regions by demonstrating preserved voltage (unipolar UpV) in segments with reduced local shortening (LS). We hypothesized that viability defined by echo and radio nuclide testing can be detected by EM during dobutamine stress.

Methods: We performed detailed EM (mean 81 points) in 6 patients with normal coronary arteries (NCA), and 31 with coronary artery disease (CAD): 14 with normal LV and 17 with impaired LV function (EF<45%). 26 patients underwent repeat EM during dobutamine infusion (5 to15 mcg/min, mean 7.1). Ectopy was more frequent during dobutamine, but adequate EM was performed (mean 71 points in < 18 min). Using echocardiography and stress-redistribution-reinjection thallium scintigraphy, 533 segments (16/map) were independently defined as: A= normal contractility without inducible ischemia, B= normal contractility with inducible ischemia, C= asynergic with preserved thallium uptake (viable/hibernating), or D= asynergic with severely reduced thallium uptake (scar).

Results: (see Table) Compared to patients with NCA, UpV and LS in ischemic and viable segments (B,C) were significantly lower. Furthermore, normal segments in CAD (A) had lower UpV than NCA patients. Compared to viable/hibernating segments (C), UpV tended to be lower, p=0.08 in scarred segments (D). Dobutamine increased LS in NCA patients, in non-ischemic (A), reversibly ischemic (B), and hibernating (C) segments (indicating contractile reserve), but not in scars (D). UpV increased with dobutamine in all segments in CAD patients and did not help discriminate viability.

Conclusion: UpV is lower in normally contracting segments in CAD compared to NCA patients, perhaps indicating subtle myocardial injury. Low-dose dobutamine mapping is feasible and may help discriminate hibernating from scarred myocardium. Table: *=p<0.05 compared to NCA, #=p<0.05 compared to baseline.

	NCA	CAD			
		A	B	C	D
UpV (mV)	19.5±7	13.7±6*	13±6*	8.8±4*	7.1±4*
LLS (%)	12.2±8	11.2±7	9.1±6*	7.4±6*	4.6±6*
Change in LLS (%)	3.5#	2.5#	2.6#	1.8#	-0.4

1184-94 ST Segment Slope Alone Detects Exercise-Induced Myocardial Ischemia in Body Surface Potential Mapping

Helena Hanninen, Panu Takala, Petri Korhonen, Lasse Oikarinen, Juha Montonen, Markku Makijarvi, Jukka Nenonen, Kim Simelius, Toivo Katila, Lauri Toivonen. *Helsinki University Central Hospital, Helsinki, Finland, Helsinki University of Technology, Espoo, Finland*

Background: Horizontal or descending configuration of the ST segment is an additional indicator of myocardial ischemia in stress ECG. We studied the capability of the ST slope to detect exercise-induced ischemia in body surface potential mapping (BSPM). **Methods:** BSPM with 123 channels was recorded in 24 single vessel coronary artery disease (CAD) patients with no previous myocardial infarction and in 17 healthy controls during supine bicycle exercise testing. Of 24 patients 11 had a stenosis in left anterior descending, 7 in right, and 6 in left circumflex coronary artery. The ST segment was defined as the second quarter from QRS offset to T wave apex. The ST slope was calculated in each recording location by fitting a regression line to the signal averaged ST segment data immediately after stress. Discriminant index, indicating the capability of each sensor site to separate a patient subgroup from other patients and controls, was calculated in each measurement location. First, the mean slope of the control group was subtracted from the mean slope of the patient subgroup. The difference was then divided by the standard deviation of the slope in all subjects. **Results:** In the CAD group and in patient subgroups the most sensitive locations for ischemia were at left inferior side below standard ECG leads V5 and V6 (ST slope CAD vs controls 285±310 vs 1060±340 uV/s; p<0.0005), and in the middle of superior back (ST slope CAD vs controls -230±250 vs -940±340 uV/s; p<0.0005). The ST slope was more horizontal in the CAD group and in the patient subgroups than in the control group (all p<0.005). In the control group the ST slope was more rapidly ascending in the anterior and more rapidly descending in the posterior thorax compared with the patient groups. With the cut off value 800 uV/s, the slope at left side separated the CAD group from controls with sensitivity of 96% and specificity of 76%. Over the back at cut of value -600 uV/s the corresponding values were 92% and 94%, respectively. **Conclusion:** In BSPM, the ST segment slope alone, without information on ST segment level, is a sensitive indicator of transient myocardial ischemia. The indicator is best exploited with BSPM, covering areas outside the conventional 12 lead ECG.

POSTER SESSION

1185 Novel Risk Markers and Therapeutic Interactions

Tuesday, March 20, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 10:00 a.m.-11:00 a.m.

1185-95 The Smoker's Paradox: Angiographic Findings and Outcome of Patients With Acute Coronary Syndromes with Respect to Smoking Status

Christopher Heeschen, Eric Boersma, John P. Cooke, Christian W. Hamm, Maarten L. Simoons. *Stanford University School of Medicine, Stanford, CA, Kerckhoff Heart Center, Bad Nauheim, Germany*

Paradoxically, tobacco use is independently associated with lower mortality in patients with acute coronary syndromes. It is assumed that this difference is due to lower plaque burden and less complex lesion characteristics in smokers. Accordingly, we investigated the database of the CAPTURE trial, which enrolled patients who had a functional single vessel disease, for angiographic findings and the clinical outcome with respect to smoking status. **Results:** 42% of the 1265 CAPTURE patients were smokers that were younger (61.0 vs. 65.1; P<0.001) and more often male (71.9 vs. 60.5%; P<0.001). During the first 24 hours prior to scheduled coronary intervention, smokers had significantly fewer coronary events (death, MI; age and gender adjusted OR 0.26; P=0.002). In contrast, their risk for PTCA-associated complications was significantly higher (adjusted OR 2.15; P<0.001). Results were similar for the 3232 PRISM patients: cardiac risk of smokers (69%) was lower during the initial 48-hour treatment period (with interventions being discouraged; adjusted OR 0.32; P<0.001) whereas in patients that were then treated interventionally, cardiac risk for smokers was elevated at 7-day follow-up (adjusted OR 3.94; P<0.001). This difference was maintained during 30-day follow-up. Baseline troponin T levels were consistently lower in smokers (0.27 vs. 0.41 µg/L; P<0.001). For the CAPTURE patients, the characteristics of the target lesions did not differ between smokers and non-smokers (P=0.86). However, baseline TIMI flow was higher in smokers with 73.5% showing TIMI 3 flow compared to 62.1% for non-smokers (P<0.001). Further, smoking status was an independent predictor of collateral flow (partial or complete retrograde filling; 16.4 vs. 8.0 %; smokers vs. non-smokers; P<0.01). **Conclusions:** After adjusting for other risk factors, smokers remained to be at lower risk during acute coronary syndromes. Despite similar lesion characteristics, they appear to have less troponin elevation, better preserved TIMI flow and a higher collateral index. The recently reported proangiogenic effect of nicotine may explain these paradoxical findings in smokers.

1185-96 The Effect of Aspirin on C-Reactive Protein as a Marker of Risk in Unstable Angina

Simon R. O. Kennon, Chris P. Price, Kulasegaram Ranjadayalan, Jackie Cooper, Heather Clarke, Peter G. Mills, Adam D. Timmis. *Barts and the London NHS Trust, London, United Kingdom*

Background: C-Reactive Protein release in acute coronary syndromes may be a response to myocardial necrosis or may reflect the inflammatory process that drives atherogenesis and predisposes to plaque rupture. Aspirin has the potential to influence C-Reactive Protein release, either directly by its antiinflammatory activity or indirectly by reducing myocardial necrosis. The clinical significance of this potential interaction has not previously been assessed.

Methods: Prospective cohort study of 304 consecutive patients admitted with non-ST-elevation acute coronary syndromes. Baseline clinical data were recorded and serial blood samples obtained for C-Reactive Protein and troponin I assay. End-points were cardiac death and non-fatal myocardial infarction during follow-up for 12 months.

Results: 174 patients (57%) were taking aspirin before admission. Patients taking aspirin had lower troponin I concentrations throughout the sampling period, only 45 (26.0%) having concentrations >0.1mg/l compared with 48 (37.8%) patients not taking aspirin (p=0.03). Maximum C-Reactive Protein concentrations were also lower in patients taking aspirin (8.16 mg/l (3.24-24.5)) than in patients not taking aspirin (11.3 mg/l (4.15-26.1)) although the difference was not significant. However, there was significant interaction (p=0.04) between prior aspirin therapy and the predictive value of C-Reactive Protein concentrations for ischaemic events (7 deaths and 21 nonfatal myocardial infarctions) at 12 months. Thus odds ratios (95% confidence intervals) for events associated with an increase of 1 standard deviation in maximum C-Reactive Protein concentration were 2.64 (1.22 - 5.72) in patients not pretreated with aspirin compared with 0.98 (0.60-1.62) in patients pretreated with aspirin.

Conclusion: The association between C-Reactive Protein and cardiac events in patients with non-ST-elevation coronary syndromes is influenced importantly by pretreatment with aspirin. The effect of aspirin on troponin release suggests that modification of acute phase inflammatory responses to myocardial injury is the major mechanism of this interaction.

1185-97 Elevated Troponin I Levels and Lesion Morphology in Unstable Angina

Jose Arias, Tien H. Nguyen, Randy Gould, Ramy Doss, Pedro Mego, Marian Hawkey, John A. Ambrose. *Saint Vincents Hospital, New York, NY*

Background: Elevated troponin levels (a sensitive marker of myocardial necrosis) in unstable angina have been shown to independently predict an adverse outcome and may be a marker for embolization to distal vascular beds. Positive correlations between ele-

vated troponin and intracoronary thrombus have been reported but thrombus was present in no more than 20% of positive individuals. Complex lesions (eccentric, irregular, overhanging edges, filling defects or ulcerations) are found in 50 to 70% of culprit lesions in unstable angina. Thus, this classification represents a more sensitive method for examining the relationship between an elevated troponin and a disrupted/thrombotic (complex) lesion. **Methods:** 162 consecutive patients undergoing coronary angiography for unstable angina with an identifiable culprit lesion and troponin I values were analyzed blindly to troponin levels obtained prior to angiography. All patients had normal creatine kinase levels. Lesions were classified according to whether or not complex or non-complex by the same angiographer who analyzed all lesions in orthogonal views blinded to clinical information. Troponin I measurements were based on MEIA technology. **Results:** See Table 1. An elevated troponin I as a predictor of a complex lesion had a sensitivity of 71%, a specificity of 70%, a positive predictive value of 71%, and a negative predictive value of 70%. **Conclusion** Thus, an elevated troponin I is a sensitive but only moderately specific marker for the presence of complex lesions confirming a relationship between thrombotic-appearing lesions and elevated troponin. However, 24 of 82 complex lesions (29%) are not associated with an elevated troponin. These data expand on prior studies suggesting that an elevated troponin may be a marker of either distal embolization of thrombotic material and/or other mechanisms resulting in transient reductions in myocardial oxygen supply leading to myocardial necrosis. Why some complex lesions do not elevate troponin requires further investigation.

	Elevated Troponin I	Normal Troponin I	P-Value
N	82	80	
Complex	58 (71%)	24 (30%)	< 0.0001
Non-Complex	24 (29%)	56 (70%)	< 0.0001

1185-98 Soluble Thrombomodulin is Elevated in Postmenopausal Women with Acute Coronary Syndromes but Is Not Associated With Adverse Outcomes nor Affected by Short Term Estrogen Therapy

Eric T. Chou, Steven P. Schulman, David R. Thiemann, Michele F. Bellantoni, Jeffrey J. Rade. *Johns Hopkins School of Medicine, Baltimore, MD, Weill Medical College of Cornell University, New York, NY*

Soluble thrombomodulin (sTM) is a marker of endothelial injury and may predict future adverse coronary events. Short term estrogen replacement therapy (ERT) has been shown to restore endothelial cell function to postmenopausal women with coronary artery disease as well as to decrease sTM levels in women without coronary disease. We retrospectively studied the effects of short-term ERT on sTM in postmenopausal women, not receiving ERT, who presented with either unstable angina or non-Q MI. Serum sTM levels were determined by ELISA in 70 postmenopausal women (mean age 69 years) with serum creatinine <2.0 mg/dl, who were randomized to receive either placebo or IV conjugated estrogen (1.25 mg) followed by oral conjugated estrogen (1.25 mg ± progesterone daily) for 21 days. Baseline sTM was compared to a cohort of 32 healthy postmenopausal age-matched controls not receiving ERT. Paired baseline and day 21 samples were available for 27 patients who were randomized to placebo or short term ERT. All patients were followed clinically for six months. **Results:** Baseline sTM in patients with acute coronary syndromes was significantly elevated compared to healthy age-matched controls (4.8 ± 2.4 vs. 3.1 ± 0.9 ng/ml, p<0.001, respectively). Baseline sTM did not correlate with recurrent ischemia, as assessed by holter monitoring, nor was it associated with the combined endpoints of death, recurrent MI, or need for revascularization over a six month follow-up period. Furthermore, short term ERT did not significantly alter sTM levels compared to baseline (delta sTM= 0.2 ± 1.4 ng/ml for the estrogen group (n=16) vs. -0.2 ± 1.0 ng/ml for placebo (n=11), p=0.3). **Conclusion:** Soluble thrombomodulin is elevated in postmenopausal women with acute coronary syndromes but is not associated with adverse cardiac outcomes nor significantly altered by short term estrogen therapy.

1185-99 Acute Coronary Syndrome Is Not Local Vascular Accident, but Pan-Coronary Process

Takayoshi Ohba, Kyoichi Mizuno, Kouji Seimiya, Masamichi Takano, Shinya Yokoyama, Ryuta Uemura, Shunta Sakai, Yoshiki Kusama, Takeshi Ino, Noritake Hata, Takurou Shinada, Yasuhiro Hiarasawa, Jun Tanabe, Kenichirou Tajika, Hiroyuki Kamon. *Cardiovasclar Medicine,Chiba Hokusou Hospital,Nippon Medical School, Inba Chiba, Japan*

Background; Recently it has been suggested that infection and/or inflammation cause plaque disruption or endothelial damage that result in thrombus formation and lead to acute coronary syndrome. Therefore, we hypothesized that the pathophysiologic process e.g. coronary thrombi, exsisted in pan-coronary arteries if the infection and/or inflammation induced the acute coronary syndrome. As angioscopy is more sensitive method to identify coronary thrombi than angiography, we performed coronary angioscopy to clarify this hypothesis. We also studied patient's recent history of infection. **Methods;** Coronary angioscopy was performed in both culprit lesions and non-ischemic related vessels in 33 patients with acute coronary syndrome and 29 patients with stable angina. All patients were questioned about infectious conditions presenting one month before angioscopy and tested for WBC, including its segment, and CRP levels on admission. **Results;** Coronary thrombi in culprit lesions were observed more frequently in patients with acute coronary syndrome than in those with stable angina (76% vs 24%,p<0.01). Moreover, thrombi in non-ischemic related vessels were more common in patients with acute coronary syndrome than in those with stable angina (61% vs 28%,p<0.05). There was no significant difference in the percent diameter stenosis in non-ischemic related lesions between this two groups. The frequency of patients who had inflammatory symptoms before angioscopy was higher in patients with acute coronary syndrome than in those with stable angina (42% vs 21%,p<0.10). On the other hand, plasma CRP levels and plasma WBC count, especially neutrocyte and monocyte, were higher in acute coronary syndrome than stable angina. **Conclusions;** Coronary thrombi exsisted in nonischemic related vessels as well as culprit lesions in patients with acute coronary syndrome. These results indicate that acute coronary syndrome is not a local vascular accident, but a pan-coronary process. Infection and/or inflammation play an important role in the outbreak of acute coronary syndrome.

1185-100 Antibiotics Against Chlamydia Pneumoniae and Helicobacter Pylori Reduce Further Cardiovascular Events in Patients With Acute Coronary Syndromes

Adam F. M. Stone, Michael Mendall, Juan-Carlos Kaski, Sandy Gupta, John Camm, Timothy Northfield. *St George's Hospital Medical School, London, United Kingdom*

Background: Infection with Chlamydia pneumoniae (Cp) and Helicobacter pylori (Hp) has been associated with coronary heart disease (CHD). We conducted a randomized, placebo-controlled intervention trial to determine the effects of antibiotics (effective against Cp and Hp) on serum inflammatory markers and major adverse cardiac events (MACE) in patients with acute coronary syndromes (ACS). **Methods:** The study enrolled 325 subjects presenting with ACS. Patients were randomized to one of 3 treatment regimens, each lasting 1 week: 1). Azithromycin 500mg od, Omeprazole 20mg bd, Metronidazole 400mg bd. (Anti-Cp) 2). Amoxycillin 500mg bd, Omeprazole 20mg bd, Metronidazole 400mg bd. (Anti-Hp) 3). Placebo Changes in serum antibody titres of Cp and Hp, inflammatory markers (CRP, fibrinogen and white cell count) and MACE (readmission with ACS, coronary revascularisation or cardiac death) were recorded. Follow-up period extended to 12 months. All patients received standard treatment for CHD. **Results:** All three groups were matched for age and classical risk factors. There was no difference in frequency or timing of MACE between either the azithromycin or the amoxycillin treated groups compared with placebo. However, when combined, subjects receiving either one or other active antibiotic treatment regimens had a 40% reduction in MACE compared with placebo (p=0.034). The full benefit was observed by 12 weeks and persisted to 1 year. No differences in inflammatory markers were noted. Cp or Hp infection status had no effect. **Conclusion:** Short courses of combination antibiotics, given to patients presenting with ACS, are associated with better clinical outcome for up to 1 year, independent of infection status. A larger trial is now merited to confirm these novel findings and to evaluate whether the benefits are related to 'antimicrobial' or 'anti-inflammtory' properties of antibiotics.

POSTER SESSION

1186 Combination Approaches to Treating Acute Myocardial Infarction

Tuesday, March 20, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 10:00 a.m.-11:00 a.m.

1186-75 Thrombolytic Therapy and the Future Risk of Stent Thrombosis

Raef H. Hajj-Ali, Stephen Green, Rana Z. Ezzeddine, Barry Kaplan, Donna Marchant, Larry Ong, Stanley Katz. *North Shore University Hospital, Manhasset, NY*

Background: Thrombolytic therapy has made a significant difference in the management of patients with acute myocardial infarction. Nevertheless, there is some concern regarding a rebound hypercoagulability state following its administration. In this era of frequent use of stents in rescue percutaneous revascularization, an increase rate of stent thrombosis following thrombolytic therapy is a concern. We thought to investigate whether patients undergoing stent implantation have an increased risk of stent thrombosis if they received thrombolytic therapy within 24 hours prior to their intervention.
Methods: The study population consisted of 5978 patients that underwent stent implantation at our institution between January 1, 1998 and June 30, 2000. Patients were followed for at least one month following their procedure and information regarding repeat hospitalization and cardiac procedures was collected. All patients were placed on aspirin and ticlopidine or clopidogrel. The primary endpoint of the study was angiographically documented stent thrombosis.
Results: The incidence of stent thrombosis in the 188 patients who received thrombolytic therapy within the 24 hours preceding their stent procedure was 4.3% (8 patients) compared to 1.2% (67 patients)in the 5790 patients that did not (p=0.001). After adjusting for post acute myocardial infarction status using logistic regression analysis the association between thrombolytic therapy and stent thrombosis was not statistically significant. Post myocardial infarction status was a strong independent predictor of stent thrombosis (OR:2.5, p=0.002).
Conclusion: The risk of stent thrombosis is increased in patients having their stent procedure within 24 hours of thrombolytic therapy. The increased risk in these patients is attributable to their post myocardial infarction status.

1186-76 Risk of Major Bleeding in Patients Treated With PTCA Early Following Thrombolysis With TNK vs. t-PA

John H. Alexander, Xin Li, Richard Chin, Hal Barron, Christopher B. Granger, Paul W. Armstrong, Frans Van de Werf. *Duke University Medical Center, Durham, NC*

Background: Although often unavoidable, PTCA following thrombolysis is associated with a risk of bleeding and ICH. This risk may be even greater with the use of glycoprotein IIb/IIIa inhibitors. We investigated risk of bleeding associated with PTCA in the set-

ting of thrombolysis and to determine whether this risk differs with different thrombolytic regimens. **Methods:** ASSENT 2 was a randomized, double-blind, 16,949 patient trial that compared the safety and efficacy of the thrombolytics TNK and t-PA in the treatment of acute myocardial infarction. We investigated the incidence of 30-day mortality, intracranial hemorrhage (ICH), major bleeding and transfusion in patients who underwent PTCA (with or without stenting) within 1 day of TNK compared to t-PA. **Results:** The patient populations were balanced with respect to age, Killip class on presentation, heart rate, blood pressure, and weight. Anterior infarcts were slightly more frequent in the t-PA group.

	TNK n=640	tPA n=598	p-value
30-day Mortality	5.3%	4.5%	0.60
ICH	0.47%	0.33%	1.0
Major Bleeding	10.6%	11.7%	0.41
Transfusion	8.8%	9.4%	0.76

Conclusion: Major bleeding and transfusion rates are relatively high in patients who undergo PTCA within 1 day of thrombolysis, however, ICH is rare. TNK is not associated with a higher bleeding risk than tPA. These results are consistent with the lower overall rate of bleeding with TNK seen in ASSENT-2.

1186-77 Impact of Stent Use Following Thrombolytic Administration on the TIMI Myocardial Perfusion Grades in Acute MI

C. Michael Gibson, Kenneth W. Baran, Michael Nguyen, George R. McKendall, Costas T. Lambrew, Gary Dykstra, Sebastian Palmeri, Lily L. Luu, Colin A. Hynes, Steve G. Gourlay, Hal V. Barron. *University of California San Francisco, San Francisco, CA, Rhode Island Hospital, Providence, RI*

Background: Stenting has been shown to increase epicaridal flow in AMI, & the goal of this study was to quantitate improvements in myocardial perfusion. **Methods:** Data are from the LIMIT trial of rhuMAb CD18 (anti WBC ab) in AMI. Adjunctive stenting was done at the discretion of the investigator. The Myocaridal Perfusion Grade (MPG) was assessed & digital subtraction angiography (DSA) was used to quantify brightness of the myocardial blush. **Results:** TIMI 3 flow was 54.2% (64/118) pre stent, & 87.2% post (102/117)(p<0.001) & TIMI frame counts decreased from medians of 37.6 to 21 (p<0.001). By DSA, there was a trend toward brighter blush post-stent than pre (8.4 ± 8.7 Gray, n=68 vs 6.8 ± 8.5, n=68, p=0.16). However, post-stent blush was not as bright as blush in normal pts without coronary syndromes (10.9 ± 5.7, n=65, p=0.001). **Conclusion:** Adjunctive stenting in AMI improves epicardial TIMI 3 flow & TIMI frame counts as well as dye inflow into the myocardium: MPG 0 is reduced & myocardial blush measured quantitatively by DSA tends to be brighter. However, dye outflow is impaired (more MPG 1 or dye staining present on next injection), possibly due to embolus, spasm or capillary leak.

TIMI Myocardial Perfusion Grade Pre and Post-stent

	Pre-PCI	Post-stent	p-value
MPG 0	25.2%, 29/118	14.3%, 16/118	0.03
MPG 0.5	19.3%, 23/118	21.9%, 26/118	NS
MPG 1	13.5%, 16/118	28.6%, 34/118	0.004
MPG 2	5.9%, 7/118	6.7%, 8/118	NS
MPG 3	36.1%, 43/118	28.6%, 34/118	0.21

5 way p-value = 0.02. MPG 0=no blush; MPG 0.5=minimal blush; MPG 1=stain on next injection; MPG 2=blush intense at injection end, gone next injection; MPG3= normal blush or ground glass appearance of myocardium.

1186-78 Adjunctive Thrombolytic Therapy With or Without Glycoprotein IIb/IIIa Inhibition Prior to Percutaneous Coronary Intervention in Acute Myocardial Infarction

Steven B. H. Timmis, Gerald C. Timmis, Michael S. Flynn, Mark C. Pica, Simon R. Dixon, Robert B. Tober, William W. O'Neill. *William Beaumont Hospital, Royal Oak, MI, Naples Community Hospital, Naples, FL*

Background: While percutaneous coronary intervention (PCI) following thrombolytic therapy has produced mixed and unsatisfying results, the adjunctive administration of glycoprotein (GP) IIb/IIa inhibitors with half-dose retavase may improve subsequent primary PCI outcomes.

Methods: 160 patients admitted to one of three community hospitals in Naples, Florida with acute MI were enrolled into this registry. Forty-seven patients were treated with half-dose retavase and IV GP IIb/IIIa inhibitors (operator's choice) while 113 subjects received IV GP IIb/IIIa inhibitors alone. Patients subsequently underwent urgent cardiac catheterization.

Results: Baseline demographics were similar for both groups. Time from treatment to cardiac catheterization was unaffected by group assignment (~140 min). Preliminary angiographic data demonstrated TIMI 2-3 patency in 61% of patients treated with combined retavase/GP IIb/IIIa inhibitor compared to 44% of those who received GP IIb/IIIa inhibitors alone before PCI (p = .147). Following PCI, 100% of patients in both groups achieved TIMI 2-3 patency. The final percent stenosis was 9.5% in the group receiving combined therapy compared to 11.4% in the cohort treated with GP IIb/IIIa inhibitor alone (p = .442). Left ventricular ejection fraction was 51% vs. 52%, respectively (p = .458).

Conclusions: This initial experience suggests that combined half-dose thrombolytic therapy and GP IIb/IIIa inhibition before primary PCI for acute myocardial infarction enhances early reperfusion compared to pretreatment with GP IIb/IIIa inhibitors alone. The final angiographic results after primary PCI were equally good with both treatment strategies.

1186-101 Both Stent and Abciximab Use During Primary Angioplasty Independently Improve Outcomes in Diabetics With Myocardial Infarction

Satyendra Giri, Joseph Mitchel, Jeffrey A. Hirst, Daniel B. Fram, Michelle Fitzpatrick, Daniel I. Simon, Francis J. Kiernan. *Brigham and Women's Hospital, Boston, MA, Hartford Hospital, Hartford, CT*

Stent and abciximab use during primary angioplasty (PA) can reduce MACE (Major Adverse Cardiac Event = death, MI, target vessel revascularization [TVR], which is particularly high in patients with adult-onset diabetes [DM]). To identify the independent effect of adjunctive therapies, we prospectively studied (01/96-01/00) 810 MI patients (DM=151) who underwent PA <12 hours of symptoms and an ECG diagnostic of MI. Quantitative coronary analysis was performed by 2 angiographers. Pre-specified clinical variables were entered in a dedicated database. Risk of explanatory variables was quantified by logistic regression modeling.

Results: The DM patients were more likely to be women (38 vs 29%), hypertensive (65 vs 43%), obese (43 vs 30%), sedentary (78 vs 65%), age >65 years (49 vs 38%), with peripheral vascular disease (16 vs 7%) and 3-vessel disease (42 vs 34%); but less smokers (32 vs 51%) or family history of premature coronary disease (20 vs 38%) vs nonDM patients (all p <0.05).

Of 151DM patients, 46 (30.4%) suffered 52 (35%) MACE (17 death, 9 MI, 26 TVR) in 6 months compared to 23.7% MACE in nonDM patients. See table for multivariate predictors. Other univariate predictors of MACE in CM patients were u-albuminuria (70 vs 51%), renal failure (16 vs 22%) and age >65 years (61 vs 44%). DM patients with MACE also presented with higher serum glucose, potassium, BUN and HbA_{1c} levels.

Conclusion: During PA, a minimal lumen diameter-MLD >2 mm, stent and abciximab use independently provide decrease MACE, which persists even after adjusting for other potent risk factors prevalent in the DM population.

Independent Predictors	Wald	Odds Ratio	95% CI
MLD >2 mm	4.51	0.25	0.07-0.89
Abciximab use	9.03	0.25	0.10-0.62
Stent Use	3.93	0.36	0.13-0.98
% Diameter Stenosis	7.72	1.11	1.05-1.17
Total Ischemia Time	17.81	1.37	1.10-1.71

1186-102 Safety and Feasibility of Abciximab Treatment in Rescue Angioplasty

Giuseppe Musumeci, Anna Sonia Petronio, Roberto Baglini, Ugo Limbruno, Giovanna Mengozzi, Giovanni Paterni, Paolo Caravelli, Mario Mariani. *CardioThoracic Dpt University of Pisa, Pisa, Italy*

We evaluated the feasibility and safety of abciximab administration in patients (pts) with acute myocardial infarction (AMI) already submitted to intravenous thrombolysis (IT) and its influence on clinical outcome. **Methods:**Seventy-seven out of 83 consecutive pts (58 male; mean age 62.5±10.6 yrs) with AMI and unsuccessful IT, submitted to rescue coronary angioplasty (PTCA) within 24 hours, were studied. Thirty pts (Group A: 38.9%) were treated with abciximab before the procedure according to the standard protocol (0.25 mcg/kg bolus plus 12-hour infusion at 0.125 mcg/min) while forty-seven pts didn't recive abciximab therapy (Group B). In Group A an intravenous heparin bolus, not followed by a continuous intravenous infusion, was administered based on body weight (70 U/kg). Major bleeding and minor bleeding were taken into account. Major adverse cardiac events (MACE) studied during the hospital stay and the 6-month follow-up were death, reinfarction, congestive heart failure, target lesion revascularization, and recurrent ischemia. **Results:** Time to reperfusion was 10.5±8 hrs; mean time interval from IT to receiving abciximab was 8.2 hrs (range 2.9 to 22); in 54 pts (70%) a stent was deployed. Rescue PTCA was successful in 96.1% of pts (96.6% in Group A and 95.7% in Group B) . In-hospital death occurred in 9.09% of pts. No difference in baseline parameters was observed between the two groups. Major bleeding occurred in two pts who didn't undergo abciximab therapy. Minor bleeding complications occurred in four pts of Group A (13.3%) and in four of Group B(8.5%; p = ns) At 30-day follow-up, only 3.3% of Group A pts presented MACE compared with 21.2% of Group B pts (p < 0.01). At 6-month follow-up, 10% of Group A pts had MACE versus 48.9% of Group B pts (p < 0.001) At 1-month follow-up, the 2D-echocardiographic evaluation showed a reduction in wall motion score index (WMSI) in 26 abciximab-treated pts (86.6%)and in only 22 Group B pts (46.8%; p < 0.05). **Conclusions:** Treatment with abciximab and low-dose heparin after IT is safe, feasible and improves the outcome of pts submitted to rescue PTCA.

ORAL CONTRIBUTIONS

855 Secular Trends in the Management of Acute Myocardial Infarction

Tuesday, March 20, 2001, 10:30 a.m.-Noon
Orange County Convention Center, Room 230D

10:30 a.m.

855-1 Medication Errors and Outcomes With Fixed Double-Bolus r-PA Versus Bolus Plus Weight-Adjusted Infusion t-PA Fibrinolysis: The GUSTO-III Experience

Shaun G. Goodman, Aiala Barr, Christopher Granger, Magnus Ohman, Anatoly Langer, Paul Armstrong, Brian Gibler, Eric Topol. *Canadian Heart Research Centre, Toronto, ON, Canada, Duke University Medical Center, Durham, NC*

Background: It has been suggested that fibrinolytic dosing errors result in higher rates of intracranial hemorrhage (ICH) and death and use of bolus lysis may reduce errors and lead to improved outcome; however, the relationship between dosing error and outcome has also been reported to be primarily due to confounding factors rather than to the dosing error itself. A small retrospective review (n=500) comparing r-PA (fixed double-bolus) and t-PA (bolus + weight-adjusted infusion) found fewer errors with r-PA, but a similar comparison derived from the only large randomized trial (GUSTO-III; n=15,059) examining patient (pt) outcomes has not been reported.
Methods: Medication errors in pts who received study lytic (n=14,766) in GUSTO-III were defined for (1) r-PA = early discontinuation (discont.); or, duration between the 1st and 2nd boluses <25 minutes (min) or >35 min; (2) t-PA = early discont.; or, dose administered either less than or greater than dose expected (based on pt weight, maximum 100 mg).
Results: Adverse outcome was higher in patients with early discont., incorrect dose (with t-PA), or incorrect duration between boluses (with r-PA)(see Table). While medication errors occurred more frequently in the t-PA vs. r-PA group (26.8% vs. 7.4%, p<0.0001), the rates of stroke (2.2% vs. 2.4%), ICH (0.7% vs. 1.0%), in-hospital (10.5% vs. 9.9%) and 30-day mortality (11.4% vs. 10.7%) were similar between the two lytic treatment error groups (t-PA vs. r-PA, all comparisons p>0.6).

Medication Error*		t-PA (n=4,834)		r-PA (n=9,932)	
		Yes* (n=1,294)	No*	Yes* (n=737)	No*
Early discontinuation*	30 day death	38.5%	6.3%	49.4%	7.0%
	Stroke	8.8%	1.6%	7.8%	1.6%
Incorrect dose/duration*	30 day death	11.1%	5.5%	10.6%	7.1%
	Stroke	2.1%	1.7%	2.3%	1.6%

Conclusions: While medical error analyses are confounded (e.g. early discont. in pts who die is not really a medical error), randomized trial data remains the best way to examine the impact of different lytic strategies on clinical outcomes. In GUSTO-III, regardless of which lytic was used, medication errors were associated with worse outcomes. However, increased rates of errors seen with t-PA were not associated with higher adverse event rates when compared with r-PA.

10:45 a.m.

855-2 High-Risk Direct Infarct Intervention Using IABP Support: Does It Make a Difference?

Robert M. Siegel, Ambika Bhaskaran, Warren Breisblatt, Barbara Barker, Alvin Nuttall, Deborah Frazier, Jennifer Vermillion, Greg Etts, Scott Olson, Jennifer Carson. *Advanced Cardiac Specialists, Gilbert / Phoenix, AZ*

Background: Clinical outcomes in acute MI have shown encouraging improvement since the advent of direct coronary intervention (d-PTCA). The challenge of d-PTCA in high-risk clinical subsets persists. Adjunctive IABP use for mechanical circulatory support in high-risk d-PTCA may improve outcomes by decreasing pre- and after-load, promoting hemodynamic stabilization and diastolic augmentation of flow through the infarct-related artery, leading to reduced remodeling and improved LV function in the long term. **Methods:** We compared acute and long-term clinical outcomes in 1,037 high-risk (TIMI criteria) patients who underwent d-PTCA within 12 hours of onset of acute MI. Of them, 430 (41%) received IABP and 607 did not (non-IABP group). The incidence of cardiogenic shock was higher (20% vs 1.5%; p<0.0001) and mean global LVEF was lower (38.1% vs 46.4%; p<0.0001) in the IABP group. Hypertension (p=0.009) was more frequent in the non-IABP group. Both groups were well-matched for all other clinical and angiographic variables. **Results:** Procedural success was higher in the IABP group (99% vs 96%; p=0.004). In-hospital complications were lower in the IABP group (p<0.001), although mean hospital stay was longer (4.3 vs 2.6 days; p<0.001). During follow-up (mean 11.3 months), target lesion revascularization rates were comparable (11.6% IABP vs 9% non-IABP; p=0.39). Mortality was significantly lower (2.3% vs 6.1%; p=0.02) and cardiac event-free survival significantly higher (86% vs 80%; p=0.045) in the IABP group. Mean rise in LVEF was higher in the IABP group (8% vs 4%; p=0.012). **Conclusions:** In this series of d-PTCA in a high-risk subset, patients with more severe/unstable presentation received IABP support. Despite this, the IABP group demonstrated significantly higher procedural success, lower in-hospital complications and lower incidence of MACE during long-term follow-up. This translated into significantly greater survival in the IABP group. These findings may have important implications for future management strategies in high-risk d-PTCA. The myriad benefits of IABP appear to be critical not just for improved in-hospital outcomes, but also for long-term absolute and event-free survival.

11:00 a.m.

855-3 National Trends in the Use of Beta Blockers for the Treatment of Older Patients After Acute Myocardial Infarction

JoAnne M. Foody, Deron H. Galusha, Jennifer M. Lewis, Dale R. Burwen, Martha J. Radford, Harlan M. Krumholz. *Qualidigm, Middletown, CT, Health Care Financing Administration, Baltimore, MD*

Background: Despite the importance of beta blockers for secondary prevention after acute myocardial infarction (AMI), they are substantially underutilized, particularly in the elderly. HCFA's quality performance measurement program provides a unique opportunity to describe current national trends of beta blocker prescription at hospital discharge among older patients with AMI.
Methods and Results. We identified two national cohorts of 30,795 and 3873 Medicare AMI cases discharged alive without contraindications to beta blocker in 1994-1995 and 1998-1999 respectively. In the 1998-1999 cohort; 71% were prescribed a beta blocker as a discharge medication compared with 50% in the 1994-1995 cohort. There was significant variation by age ranging from 60% to 75% (p < 0.001 for trend). In general, the very old (≥85) are less likely to be prescribed beta blockers (60% vs. 73%, p < 0.001 for trend).
Conclusions. Currently, more than one quarter of ideal elderly patients do not receive beta blockers as part of their discharge medications. Patients ≥ 85 free from contraindications continue to be less likely to receive beta blockers than their younger counterparts. While there has been an absolute improvement in beta blocker use across all age groups nationally, this improvement relative to the opportunity was the smallest in those ≥ 85. Despite continued improvement in national beta blocker usage following AMI, many ideal older patients do not receive this important and effective therapy.

National Trends in the Use Of Discharge Beta Blockers In Older Patients After AMI

AGE	1994-1995 Prescribed/Ideal (%)	1998-1999 Prescribed/Ideal (%)	Change in Rate
<65	1408/2660 (52.9)	303/403 (75.2)	22.3
65-74	7633/14078 (54.2)	1130/1529 (73.9)	19.7
75-84	5025/10497 (47.9)	964/1346 (71.6)	23.7
>/= 85	1339/3560 (37.6)	357/595 (60.0)	22.4
ALL	15405/30795 (50.0)	2754/3873 (71.1)	21.1

11:15 a.m.

855-4 Higher Coronary Intervention Following Acute MI Associated With Lower Rates of Evidence-Based Medical Therapy in Regions of North America: Results From ASSENT II

Maria Cecilia Bahit, John H. Alexander, Gudaye Tasissa, Paul W. Armstrong, Robert M. Califf, Christopher B. Granger. *Duke Clinical Research Institute, Durham, NC*

Background: Randomized clinical trials and clinical practice guidelines have provided clear evidence that certain medications improve survival in patients with ST elevation myocardial infarction (MI). The aim of this study was to determine whether the use of evidence based medications and procedures differ across North America (NA) for patients with ST elevation MI. **Methods:** Using the database of the ASSENT II trial, which compared TNK vs t-PA in patients with MI, we selected patients enrolled in N.A. We examined the use of aspirin, beta-blockers (bb), ACE inhibitors, coronary angiography and angioplasty, length of stay (mean LOS, days) among census regions across United States (US) and Canada. **Results:** Of the 16949 patients in ASSENT II, 4806 (28 %) patients were enrolled in North America between October 1997 and November 1998. Baseline characteristics were similar across the regions. The use of aspirin was uniformly high (from 95% to 97%). The use of cardiac procedures generally was inversely related to the use of evidence-based medications.For example, the central US had the highest rate of PCI, lowest use od beta-blockers and ACE-I, and shorter LOS.On the other hand, Canada and New England had the highest use of ACE-I and beta-blockers, respectively.

	West Central n=406	East Central n=676	Mid Atlantic n=687	South Atlantic n=981	West n=653	New Eng n=289	Canada n=1114	p
PCI	53%	49%	48%	47%	45%	38%	13%	0.001
bb	82%	89%	92%	87%	84%	92%	85%	0.001
ACE-I	45%	42%	51%	48%	50%	47%	52%	0.001
LOS,days	5.9	5.8	7.8	6.5	6	6.3	7.8	0.001

Conclusion: There was wide variation in both coronary interventions and the use of evidence-based medicine in North America in the treatment of acute MI, and regions with higher intervention rates had both shorter hospital length-of-stay and lower use of proven medical therapies.

11:30 a.m.

855-5 National Trends in Quality of Care for Acute Myocardial Infarction (AMI) Between 1994-1995 and 1998-1999

Dale R. Burwen, Deron H. Galusha, Jennifer M. Lewis, Harlan M. Krumholz, Marjorie R. Bedinger, Martha J. Radford. *Health Care Financing Administration, Baltimore, MD, Qualidigm, Middletown, CT*

Background: Many studies have documented underuse of recommended therapies for AMI patients. Information about the change in use of these therapies over time is critical to evaluate and target quality improvement efforts. We report the first national trend data for AMI care from the Medicare Health Care Quality Improvement Program.

Methods: A national sample of medical records of Medicare AMI hospitalizations during an 8-month period in 1994-1995 (n=234754) and a 6-month period in 1998-1999 (n=35713) was abstracted. We determined the percent of cases receiving key therapies (after excluding patients with contraindications), the change in use over time (from 1994-1995 [baseline] to 1998-1999), and change relative to the opportunity for improvement (100% - baseline rate).

Results: Median utilization (25^{th},75^{th} percentile) by state is shown:

Quality Indicator	1994-1995 % utilization	Absolute change %	Relative change %
Early administration of aspirin	77 (76,80)	_7_(5,9)	31 (23,39)
Aspirin prescribed at discharge	79 (76,82)	_6_(3,8)	27 (16,35)
Early administration of beta-blocker	50 (43,56)	19 (14,22)	39 (32,44)
Beta-blocker prescribed at discharge	50 (42,54)	22 (18,28)	44 (36,52)
ACE inhibitor for systolic dysfunction	63 (60,68)	7 (3,11)	20 (7,32)
Smoking cessation counseling	43 (39,49)	_-3 (-8,4)	-5 (-14,8)

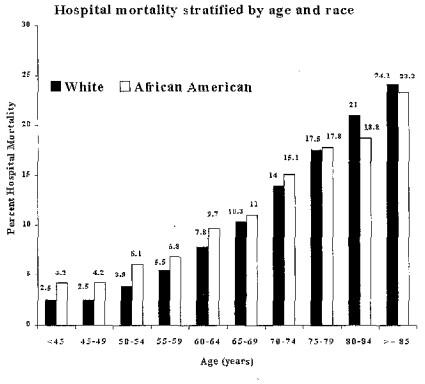
Conclusions: Over a 4 year period, varied progress was made across care processes (beta-blockers > aspirin ≥_ACE inhibitors; no improvement in documented smoking advice) and states. Important advances were made, however, diffusion into practice can be a slow process. In the meantime, a significant proportion of Medicare patients hospitalized with AMI are not receiving optimal, evidence-based therapies to reduce mortality.

11:45 a.m.

855-6 Higher Early Mortality Among Younger African Americans After Myocardial Infarction: Analysis of the National Registry of Myocardial Infarction-2

Ajay Manhapra, John G. Canto, Viola Vaccarino, Lori Parsons, Hal V. Barron, Nathan R. Every, Catarina A. Kiefe, William J. Rogers, W Douglas Weaver, Steven Borzak. *Henry Ford Heart and Vascular Institute, Detroit, MI, University of Alabama at Birmingham Medical Center, Birmingham, AL*

Background. Young African Americans with acute myocardial infarction reportedly have higher short-term mortality than Whites of similar age. However, the relationship of younger age with increased short-term mortality in African Americans, and the influence of demographic, clinical and treatment factors on this relationship have not been explored in detail. **Method.** We analyzed the patient characteristics and mortality data of 558,272 patients enrolled in the National Registry of Myocardial Infarction-2 who were 90 years or younger and had confirmed myocardial infarction (40,903 African Americans and 501,995 Whites). **Results.** The overall mortality was slightly lower among African Americans compared to Whites (10.9% in blacks and 12.0% in whites, p<0.0001). The mortality of African Americans younger than 65 years of age was significantly higher compared to Whites of similar age groups (figure). Logistic regression analysis showed that younger age had a negative influence on the mortality of African Americans compared to Whites (p value for age-African American race interaction on mortality <0.0001). Each 5 year decrement in age was associated with 7.2% higher odds of death in African Americans (95% confidence intervals 5.7% - 7.6%) compared to Whites. Although there was substantial variation between African Americans and Whites in different patient characteristics, these variations were found to account for only a quarter of the higher risk of death in African Americans on multivariate analysis (5.4% increased odds for death after adjustments, 95% confidence intervals 3.6% - 7.2%). **Conclusion.** Younger African Americans have a higher short-term mortality compared to Whites of similar age following an acute myocardial infarction.



POSTER SESSION

1216 Stabile Ischemic Syndrome: Pathophysiology, Diagnosis, and Prognosis I

Tuesday, March 20, 2001, Noon-2:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 1:00 p.m.-2:00 p.m.

1216-75 Impact of Gender on the Improvement in Left Ventricular Systolic Function Following Coronary Artery Bypass Graft Surgery for Ischemic Cardiomyopathy

Mohammad Bashir, Imran Afridi, Ibrahim Abdalla, Nicholas G. Smedira, Eugene Blackstone, Michael S. Lauer. *The Cleveland Clinic Foundation, Cleveland, OH*

Objective: It is known that left ventricular systolic function improves in patients with ischemic cardiomyopathy (ICM) undergoing coronary artery bypass graft surgery (CABG). We sought to study the impact of gender on the improvement in left ventricular ejection fraction (LVEF) following CABG in patients with ICM. **Methods:** We reviewed CABG database at our institution from 1990-97 and identified patients with LVEF <40% who underwent isolated CABG and had echocardiography within 6 months prior to and 12 months after CABG. Multivariate linear regression analysis was performed to identify independent predictors of improvement in LVEF. **Results:** Study population included 516 patients (128 females, mean age 65 ± 11 years). Although female patients were older (67 ± 10 years vs. 63 ± 11 years, p=0.003), they had a significantly higher pre-operative LVEF compared with male patients (30 ± 7% vs. 28 ± 7%, p=0.004). Following surgery, LVEF continued to be significantly higher in female patients (34 ± 11% vs. 30 ± 9%, p<0.0001). A higher percentage of women had a significant improvement in LVEF (>10%) than men (30.5% vs. 21.9%, p<0.05). There was a greater absolute increase in LVEF (ΔEF) in female patients (4 ± 11% vs. 1.5 ± 9%, p=0.01). After adjusting for age, diabetes, history of smoking, prior myocardial infarction, pre-operative LVEF, number of stenosed coronary arteries and number of arterial bypass grafts, female gender remained associated with a significantly higher ΔEF.
Conclusions: A higher percentage of women than men had a significant improvement in left ventricular systolic function following coronary artery bypass graft surgery for ischemic cardiomyopathy. Furthermore, the absolute increase in left ventricular ejection fraction was more in women.

1216-76 Myocardial Stunning Severity Is Related to the Intensity of Ischemia in Patients With Coronary Artery Disease

Edward Barnes, David P. Dutka, Roger J. C. Hall, Paolo G. Camici. *National Heart and Lung Institute at Hammersmith Hospital, London, United Kingdom*

Background: It is well established from animal models that the severity of myocardial stunning is related to the degree of the preceding episode of ischemia. Using dobutamine-induced ischaemia in patients with angiographically proven coronary artery disease (CAD) and stable angina pectoris, we assessed the relationship between the degree of post-ischemic left ventricular (LV) dysfunction (echocardiography), the severity of coronary stenosis (angiography) and peak myocardial blood flow (MBF) measured with positron emission tomography (PET) and oxygen 15-labeled water. **Methods:** 14 patients (61±7 years) with normal resting LV function were studied(ejection fraction 64±5%). Regional systolic function (shortening fraction [SF]) was assessed at baseline and regular intervals after dobutamine. MBF was measured at baseline, peak stress and after stress just prior to the 30 minute echo data acquisition. **Results:** Global reversible post-ischemic LV dysfunction, that had recovered 60 minutes after peak stress, occurred in 9 of the 14 patients. In these 9 patients, there was no difference in regional MBF (corrected for rate pressure product) at baseline and 30 minutes after dobutamine when LV function was impaired, but subsequently recovered, confirming stunning. Moreover, the severity of stunning was related to the severity of the coronary stenosis and to MBF at peak stress (table). **Conclusions:** This study is consistent with previous work in animals and demonstrates that in patients with CAD the degree of myocardial stunning is related to coronary stenosis severity and to the degree of attenuation in peak MBF.

Table: Mean±SD (*=p<0.01 vs. 50-80% stenosis)

Stenosis Severity (%diameter)	SF (30mins)	p vs. baseline	Peak MBF (ml/min/g)	p vs. peak MBF <50% stenosis
<50	93.9±25	NS	2.01±0.71	
50-80	85.4±21	<0.001	1.75±0.40	=0.002
>80	67.4±25*	<0.001	1.47±0.30	=0.003

1216-101 The Influence of Diabetes and Hypertension on Microvascular Dysfunction in Chronic Total Coronary Occlusions

Gerald S. Werner, Barbara M. Richartz, Oliver Gastmann, Markus Ferrari, Hans R. Figulla. *Friedrich-Schiller-University, Jena, Germany*

Background: Microvascular dysfunction (MD) after PTCA is detected by a reduced coronary flow reserve (CFR) in the absence of a residual epicardial lesion. MD is observed with diabetes mellitus and hypertension, extensive coronary artery disease (CAD), and prior myocardial infarction (MI). In nonocclusive lesions about 20% of pts show MD. It is unknown to what extent it occurs in total chronic coronary occlusions (TCO).

Patients: Thirty patients (pts) underwent a successful recanalization of a TCO (mean duration of occlusion: 17 months (1-117). Intracoronary Doppler was used to measure average peak velocity (APV) and to assess CFR after stent placement during maximum hyperemia induced by 20µg adenosin i.c. A cut-off value of CFR<2.0 was used to discriminate pts with and without MD. Angiographic follow-up was done after 5.5±1.4 months. CFR was reassessed in all pts, in case of target lesion revascularization after the repeat PTCA.
Results: A history of hypertension was known in 57%, diabetes mellitus in 47% of pts. Multivessel disease was present in 73%, prior MI in 73%. CFR after stenting of the TCO was 1.87±0.51; and a CFR<2.0 was observed in 67%. CFR at baseline was independent of the history of MI or extent of CAD. CFR was lower in pts with hypertension and/or diabetes than without this comorbidity (1.64±0.36 vs. 2.22±0.43; p<0.001). This was due to a trend towards a lower maximum hyperemic APV with hypertension and/or diabetes (47.9±19.6 vs. 61.9±37.0 cm/s;p=0.15). At the time of follow-up, CFR had improved significantly in the whole study group. This was due to the change in patients with hypertension and/or diabetes: CFR increased to 2.63±0.99 (p<0.001 as compared to baseline). The increase in pts without comorbidity was not significant (to 2.55±0.81). At follow-up the CFR were similar in both groups, and also the basal and maximum hyperemic APV had reached a similar level.
Conclusion: The majority of pts with TCO had evidence of MD. This may be explained by the change from collateral dependent to antegrade perfusion in TCO with impairment of microvascular response in the presence of hypertension and diabetes mellitus. MD has the potential to recover over a period of several months.

1216-102 Protective Effects of a Beta Blocker on Progressive Left Ventricular Remodeling in Chronic Ischemic Cardiomyopathy With Hibernating Myocardium

Chunguang Chen, Sergei Aksenov, Huashan Hong, Jing Liu, Joseph Marak, John Fallon, David Waters.. *Newark Beth Israel Medical Center, Newark, NJ*

Background: We have previously shown that progressive LV remodeling occurs if hibernating myocardium is not reperfused. We hypothesized that although myocardial hibernation restores the delicate balance of oxygen consumption and supply in LV regions supplied by a severe coronary stenosis with minimal flow reserve, it may not protect myocardium from intermittent ischemia due to episodes of increased oxygen demand during daily activities. Unprotected ischemic episodes may contribute to the deterioration of LV dysfunction and progression of LV remodeling. Beta-blocker will decrease ischemia and prevent progressive LV remodeling in hibernating myocardium. **Methods and Results:** Three groups of 22 pigs were studied. Group 1 (n=9): Severe LAD stenosis was created with a resting coronary flow reduction of 30-40% and was maintained for 4 weeks; Group 2 (n=7): The same severe LAD stenosis was maintained for 4 weeks as in Group 1 and oral metoprolol (100 mg x 2/day) was given starting immediately after creation of the coronary stenosis. Group 3 (n=6): controls without a stenosis. Coronary flow (CF), LV wall thickening (WT) in the hibernating region, LV volume, mass and EF, and myocardial fibrosis measurements are summarized in the table:

***: p < 0.01 compared to control; #: p<0.05 compared to Group 2.**

	Group 1: 4W CAD	Group 2: 4W CAD & beta-blocker	Group 3: control
CF (ml/g/min)	0.81+/-0.11*	0.83+/-0.12*	1.21+/-0.14
WT (%)	11+/-5*	14+/-4*	39+/-3
LVEDV (ml)	145+/-25*#	125+/-19*	98+/-11
LV mass (g)	128+/-8*#	120+/-7*	95+/-4
LV EF (%)	35+/-5*	39+/-6*	58+/-3
Interstital fibrosis (%)	19+/-6*#	12+/-4*	6.2+/-3

Conclusions: Progessive LV remodeling occurred in hibernating myocardium without reperfusion. However, beta-blocker administration significantly attenuated LV remodeling and decreased myocardial fibrosis in hibernating myocardium.

POSTER SESSION

1217 Biochemical Alterations and Marker Release in the Ischemic Myocardium

Tuesday, March 20, 2001, Noon-2:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 1:00 p.m.-2:00 p.m.

1217-77 By What Mechanism Does Glucose-Insulin-Potassium Improve Survival Following Myocardial Infarction?

Dieter Lubbe, John D. Altman, Birgit Kantor, David R. Holmes, Jr., Robert S. Schwartz, Bernard J. Gersh. *Mayo Clinic, Rochester, MN*

Background: Glucose-insulin-potassium (GIK) infusion during an acute myocardial infarction improves survival. This study was performed to determine if GIK reduces microvascular dysfunction, myocardial infarct size, postischemic ventricular contractile dysfunction, and ischemia-reperfusion arrhythmias.
Methods: In 8 pigs the left anterior descending artery was occluded for 60 minutes followed by 28 days of reperfusion. GIK or placebo infusion was started at the time of occlusion. Free fatty acids (FFA) were measured to document GIK effect. Coronary flow reserve was measured at baseline and 60 minutes to assess microvascular function. Radioactive microspheres were injected during coronary occlusion to measure collateral blood flow and at 28 days for infarct size determination. Left ventricular angiography was performed at baseline and 28 days. Area at risk was determined with perfusion of Evan's Blue. TTC staining was performed as a second measurement of infarct size.
Results: GIK infusion resulted in a significant reduction in free fatty acid levels indicating a metabolic effect. GIK did not improve CFR at 60 minutes or reduce ischemia-reperfusion arrhythmias. Myocardial infarct size and left ventricular function at 28 days was unchanged by GIK infusion.
Conclusion: The study indicates that GIK does not reduce microvascular dysfunction, myocardial infarct size, ischemia-reperfusion arrhythmias, or left ventricular function.

Effects of GIK

	FFA (mg/l)	Infarct Size (%AAR)	LVEF	VT frequency%
GIK	0.2 +/- 0.1	36 +/- 5	51 +/- 11	67
Placebo	0.8 +/- 0.2*	15 +/- 14	45 +/- 14	67

*p<0.03 vs placebo

1217-78 Ischemia-Reperfusion of Rat Myocardium Activates NF-kB and Induces Neutrophil Infiltration via Lipopolysaccharide-Induced CXC Chemokine

Bysani Chandrasekar, Jeffrey B. Smith, Gregory L. Freeman. *The University of Texas Health Science Center, San Antonio, TX, UCLA School of Medicine, Los Angeles, CA*

Background: Mechanisms by which neutrophils are attracted to the myocardium following ischemia/reperfusion are not fully defined. The goals of the present study were to evaluate the roles of chemokines LIX (lipopolysachharide-induced CXC chemokine), KC (cytokine-induced neutrophil chemoattractant), and MIP-2 (macrophage inflammatory protein-2) in vivo in a rat model of reperfusion injury, and to examine the mechanisms of chemokine induction by oxidative stress and cytokines in cultured adult rat cardiomyocytes. **Methods and Results:** Male WKY rats underwent 45 minutes of LAD coronary artery ligation followed by reperfusion for various periods. Compared to sham-operated controls, myocardium from reperfused animals had: higher levels of free radicals, increased neutrophil infiltration evidenced histologically and by elevated myeloperoxidase activity, and increased NF-kappaB DNA binding activity. Ischemia-reperfusion also induced the expression of IL-1beta, TNF-alpha, LIX, KC, and MIP-2 mRNA and protein. LIX expression was localized to resident myocardial cells, whereas KC and MIP-2 were expressed only in infiltrating inflammatory cells. Neutralization of LIX inhibited 74% of neutrophil infiltration into previously ischemic myocardium. In cultured cardiomyocytes, LIX expression was induced by oxidative stress or TNF-alpha, and blocked by the NF-kappaB inhibitor pyrrolidinedithiocarbamate. **Conclusions:** The induction of LIX expression, via an NF-kappaB dependent mechanism, may be a key step in the recruitment of neutrophils to reperfused myocardium following ischemia in the rat.

1217-79 Expression of Matrix Metalloproteinase-2 (MMP 2) and Tissue Inhibitor of Matrix Metalloproteinase-2 (TIMP 2) In Vivo During Myocardial Ischemic Injury and In Vitro in Cardiac-Derived Fibroblasts and Endothelial Cells

Dolores Cortez, James Colston, Teresa Frosto, Bysani Chandrasekar, Gregory Freeman. *Univ. of Texas Health Science Center at San Antonio, San Antonio, TX*

Background: The exact role of matrix metalloproteinases (MMPs) and tissue inhibitors of matrix metalloproteinases (TIMPs) in myocardial ischemia is not completely defined. MMP2 degrades extracellular matrix, is regulated by TIMP2, and is cleaved to its active form by membrane-type matrix metalloproteinase-1 (MT1-MMP). The aims of this study were i) to evaluate MMP2, TIMP2, and MT1-MMP expression in ischemic myocardium, and ii) to determine which cardiac constituent cells express MMP2 and TIMP2 at steady state. **Methods:** Four male Wistar-Kyoto rats were sacrificed after ligation of the left anterior descending coronary artery for one hour. Ischemic myocardium was analyzed by RT-PCR for MMP2 and TIMP2 mRNA expression. MT1-MMP was localized in ischemic myocardium by immunohistochemistry. Serum MMP2 activity and TIMP2 levels were determined by enzyme immunoassay (ELISA). MMP2 and TIMP2 expression was evaluated by RT-PCR and ELISA in cardiac-derived fibroblasts and endothelial cells in vitro. Sham-operated and normal, non-operated rats served as controls. **Results:** Ischemic and control myocardium expressed MMP2, TIMP2 and MT1-MMP constituitively. MT1-MMP was detected by immunohistochemistry in ischemic and normal myocardium. Both MMP2 and TIMP2 mRNA were detected in the ischemic myocardium and controls. However, average MMP2 serum levels in ischemic rats were greater (2.05 ng/ml) than in sham (0.59 ng/ml) and normal rats (0.497 ng/ml). Average TIMP2 levels in ischemic rats were lower (105.5 ng/ml) than in sham (125.7 ng/ml) and normal animals (146.7 ng/ml). Our results also showed that MMP2 and TIMP2 expression is cell specific. In vitro studies showed that at steady state, endothelial cells produce TIMP2 but not MMP2 mRNA or protein. In contrast, fibroblasts at steady state express MMP2 mRNA and protein as well as TIMP2 mRNA but not TIMP2 protein. **Conclusion:** This study is novel in that it describes constituitive expression of MMP2, TIMP2, and MT1-MMP during cardiac ischemia and localizes the protein of MMP2 to fibroblasts and that of TIMP2 to endothelial cells. Further work is in progress to define the roles of these enzymes in myocardial remodeling.

1217-80 The Hyperthyroid Rat Heart Produces Diminished HSP 70 m RNA by Preconditioning Investigation of Mechanisms

Dennis Cokkinos, Costas Pantos, V. Malliopoulou, S. Tzeis, DD Cokkinos, N. Steimberg, H. Carageorgiou, DV Varonos. *Onassis Cardiac Surgery Center, Athens, Greece*

Background: The aim of the study was to investigate whether thyroxine (TH) administration modifies the HSP70 m RNA expression induced in response to ischemic preconditioning (PC) in the isolated rat heart. **Methods:** L-thyroxine was administered in male Wistar rats (25 lg / 100 g sc daily for 2 weeks, THYR), while rats treated with saline served as controls (NORM). Isolated hearts were perfused in the Langendorff mode and subjected after stabilization to 20 min of zero flow global ischemia (I) and 45 min of reperfusion, THYR, n=8 and NORM, n=6. PC hearts after the stabilization period, underwent 3 min of I, 5 min of R, followed by 5 min of I and 5 min of R, followed by 20 min of I and 45 min of R, NORM 2PC, n=6 and THYR 2PC, n=6. Hearts from normal and THYR rats were also subjected to additional 2 cycles of PC consisting of 5 min of I and 5 min of R, NORM 4PC, n=6 and THYR 4PC, n=6. The induction of HSP70 m RNA at 45 min of reperfusion was detected by Northern blot hybridization. Total and phosphorylated p38 MAP kinase and PKC å expression were measured by Western blot analysis. **Results:** HSP70 m RNA expression was 3-fold greater in NORM 2PC compared to NORM hearts. HSP70 m RNA induction in THYR 2PC was 2-fold less than in THYR hearts, p<0.05. In NORM 4PC hearts, HSP70 m RNA expression was increased 1.5 fold as compared to NORM 2PC hearts, p<0.05, while in THYR 4PC hearts HSP70 m RNA induction was not altered in comparison to THYR 2PC. The levels of total p38 MAP kinase were similar between the THYR and NORM hearts. However, phorsphorylated p38 MAP kinase was 2-fold lower in THYR 2PC compared to NORM 2PC hearts, p<0.05 Basal PKCå expression was 1.7 fold more in the normal as compared to the hyperthyroid hearts, p<0.05. **Conclusion:** Thyroxine administration decreases the HSP70 m RNA expression induced by ischemic preconditioning. This mechanism through diminished phosphorylation of p38 MAP kinase, because of repressed PKCå expression, is being proven for the first time.

1217-81 Predictive Value of NT-proBNP in 118 Patients With Acute Myocardial Infarction Undergoing Primary Coronary Angioplasty

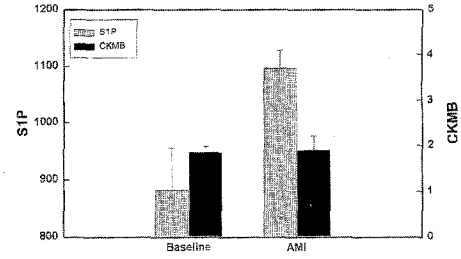
Franz S. G. Hartmann, Volkhart Kurowski, Ali Maghsoudi, Hendrik Bonnemeier, Thomas Kurz, Hugo A. Katus, Gert Richardt. *Medizinische Klinik II, UK Luebeck, Luebeck, Germany*

Background: In acute myocardial infarction predictive value of the degree of neurohumoral activation is well established. Recently, the natriuretic-peptide metabolite NT-proBNP received interest as prognostic marker, which is possibly superior to plasma catecholamines. So far, however, neither time-course nor predictive value of NT-proBNP plasma concentrations has been prospectively evaluated in patients undergoing successful reperfusion by primary PCI. **Methods:** Therefore, we conducted a prospective study in 118 consecutive patients with acute myocardial infarction receiving successful reperfusion (TIMI 2 and 3) by primary PCI. Arterial plasma levels of epinephrine, norepinephrine and NT-proBNP were determined before, 60 min and 10 days after reperfusion and compared to established postinfarction risk markers. Follow-up was performed for 18-36 months recording major cardiac events, defined as cardiac death, reinfarction, ventricular fibrillation or hospitalization for heart failure. **Results:** Catecholamine concentrations (mean±SEM) reached a maximum in the first hour of myocardial infarction (norepinephrine: 602 ±44 mg/dl, epinephrine: 213 ±24 mg/dl), but returned to nearly normal values at 10 days. In contrast, NT-proBNP levels were equally elevated at 0 and 60 min (791 ±46 mmol/l at 60 min), but further increased to 924 ±54 mmol/l at 10 days. For prediction of cardiac events, an 60 min NT-proBNP postinfarction level of >761mmol/l had sensitivity, specificity, positive and negative predictive values of 78%, 64%, 33% and 93%, respectively and was superior to any other neurohormone and to early LVEF. By multivariate analysis, NT-proBNP provided predictive information for cardiac events independent of patient age, sex, early LVEF or history of myocardial infarction. **Conclusion:** Plasma NT-proBNP measured 60 min after reperfusion was superior to plasma catecholamines and LVEF in predicting event-free survival. Stratification of patients into low- and high-risk groups can be facilitated by early plasma NT-proBNP measurements. Therefore, this natriuretic peptide should reasonably be included in the routine clinical work up of patients after myocardial infarction.

1217-82 Sphingosine-1-Phospate Is an Early Serum Marker for Acute Myocardial Infarction (AMI)

Jeffrey S. Carstens, Douglas H. Deutschman, M. Trevor Page, Robert E. Klepper, Roger A. Sabbadini. *San Diego State University, San Diego, CA, Naval Medical Center, San Diego, CA*

The MIRF (Myocardial Ischemia Rating Function) trial was a 318 patient trial designed to test the diagnostic utility of serum sphingolipids as markers for ischemia. The primary endpoints were the assessment of coronary artery stenosis by angiography and serum sphingolipids, including sphingosine-1-phosphate (S1P). For analysis, the patients were grouped by disease severity according to the number of major coronary arteries involved by stenosis. This included an 'active ischemia' group consisting of hospitalized pts found to have 2-3 vessel distribution with greater than 70% stenosis. This active ischemia group had the highest S1P level (1108 pmol/mL). Post-hoc analysis revealed that 87% (33 of 38 pts) of the active ischemia group had acute coronary syndrome (ACS) and 42% (16 of 38) had MI as a discharge diagnosis. At the time of catheterization, 10 of the MI patients had normal CKs, but had S1P levels which averaged 1097 pmol/mL which were significantly (p<.01) higher than the baseline levels (882 pmol/mL) for non-hospitalized pts with mild (<50%) coronary stenosis. It is concluded that serum S1P may be an early marker for the ischemia associated with ACS. In addition it may be useful for early diagnosis of AMI before the traditional cardiac death markers appear. This finding warrants further investigation.



1217-83 Effects of Heparin on Plasma Tissue Factor (TF) and Tissue Factor Pathway Inhibitor (TFPI) in Patients With Acute Myocardial Infarction (AMI)

Shaker A. Mousa, Jeffrey M. Bozarth, Marc Cohen, Michael F. Wilson, Mofid N. Khalil-Ibrahim. *DuPont Pharmaceuticals co., Wilmington, DE, Kaleida Health & univ. of New York, Buffalo, NY*

Background: Several studies have shown that thrombosis and inflammation play a key role in the pathogenesis of coronary artery diseases. Elevated plasma levels of tissue factor might be responsible for the thrombogenicity of the atherosclerotic plaque by initiating and amplifying thrombin generation. The aim of the present study was to determine the circulating plasma levels of TF and TFPI and to assess the effect of heparin in patients with AMI. **Methods:** Plasma samples obtained from 25 AMI patients pre- and 1-2 days during heparin (50 IU/kg, IV followed by 5000 IU x 3 for 5 days) use as well as from 12 healthy subjects were assayed for plasma TF and total TFPI using specific ELISA. **Results:** A significant elevation (* $p < 0.05$) in both TF and TFPI was demonstrated in AMI patients as compared to levels in healthy subjects. Heparin treatment was associated with a significant ($P < 0.01$) reduction in TF back to normal levels. Furthermore, heparin resulted in a significant (** $P < 0.01$) elevation in plasma TFPI by about two fold over normal levels.

Plasma Levels of TF & TFPI In AMI Patients: Effects of Heparin

Biochemical Markers	Control	AMI, Pre-Heparin	AMI, Heparin
TF (pg/ml)	140 +/- 25	255 +/- 45*	175 +/- 21
TFPI (ng/ml)	56 +/- 15	110 +/- 26*	203 +/- 55**

Data in the table represent Mean +/- SD, * $P < 0.05$, ** $P < 0.01$. **Conclusion:** Increased pro-thrombotic events in AMI patients might be related to elevated TF circulating levels not sufficiently inhibited by elevated TFPI levels. These initial results suggest potential anti-inflammatory and cytoprotective benefits of heparin via its TFPI release in addition to its known antithrombotic actions in AMI patients.

POSTER SESSION

1218 Acute Coronary Syndromes: Predictors of Long-Term Outcome

Tuesday, March 20, 2001, Noon-2:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 1:00 p.m.-2:00 p.m.

1218-84 Elevated C-Reactive Protein and Increasing Severity of Coronary Artery Disease: Independent or Interdependent Predictors of Risk?

James S. Zebrack, Joseph B. Muhlestein, Benjamin D. Horne, Tami L. Bair, Dale G. Renlund, Jeffrey L. Anderson. *University of Utah, Salt Lake City, UT, LDS Hospital, Salt Lake City, UT*

Background: C-reactive protein (CRP), a marker of inflammation, has been proposed as a new coronary risk factor. However, questions remain about the implications of an elevated CRP. Is it a surrogate for the extent of coronary artery disease (CAD), and are CRP and CAD independent or interdependent predictors of risk?
Methods: To assess the relation of CRP and CAD, we studied 2701 patients (pt) without acute myocardial infarction (MI) undergoing angiography; 1722 had severe CAD (≥1 stenosis ≥70%), 284 mild/moderate, and 695 no CAD. CAD was quantified in 6 ways: presence of severe disease; # of vessels with severe disease (>70% stenosis) or moderate/severe disease (>50% stenosis); and # of severe lesions, mild/moderate lesions (10-69% stenosis), or total lesions. CRP was measured at angiography by a high sensitivity method (Abbott). Associations between CRP and CAD were assessed by Pearson's correlation coefficient. Pt were followed for up to 5 years (mean, 2.0 ± 1.4). Associations with death and nonfatal MI were evaluated using Cox regressions (9 co-variables).
Results: Pt were 64 ± 12 years old; 68% were men. During follow-up, 174 CAD pt died and 105 had non-fatal MI. Correlations of CRP with measures of CAD were highly significant (p<.001) for all but moderate lesions, but the correlation coefficients were low (0.051-0.081). The number of pt with severe disease and number of severe vessels correlated best. Subsequent death was predicted univariately by CRP (p<.0001) and all

CAD measures (p<.0008) except moderate lesions. In bivariate analyses, significance was preserved for CRP and the 5 CAD measures. In multivariate analyses, significance was retained for CRP (p<.001), number of severe vessels (p=.002), total lesions (p=.01), and severe lesions (p=.03). Results were similar for the combined endpoint of death/nonfatal MI.
Conclusions: CRP correlated with several measures of extent and severity of CAD at catheterization, but the degree of correlation was low, suggesting the importance of additional factors. During follow-up, both CRP and selected measures of CAD retained independent predictive value. CRP and CAD correlate partially, but each retains significant independent predictive value.

1218-85 Percutaneous Intervention in Unstable Plaques: The Significance of Temperature Measurement in Prognosis

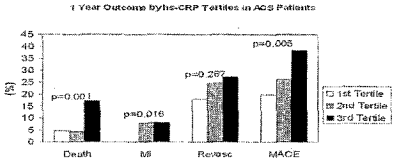
Christodoulos I. Stefanadis, Konstantinos Toutouzas, Eleftherios Tsiamis, Costas Stratos, Ioannis Kallikazaros, Manolis Vavuranakis, Costas Tentolouris, Dorothea Tsekoura, Pavlos Toutouzas. *Hippokration Hospital, Athens, Greece*

Background: Previous studies have shown that local temperature is increased in unstable angina. The aim of the present study was to evaluate the significance of increased temperature of culprit lesions in patients suffering from acute coronary syndromes, undergoing successful percutaneous intervention. **Methods:** In the study we included 56 patients, mean age 61.2±9 years, suffering from unstable angina or acute myocardial infarction. All patients underwent balloon angioplasty, in order to accomplish TIMI III flow. Thereafter, using a thermography catheter previously validated, we measured the temperature difference (ΔT) between the atherosclerotic plaque and the healthy vessel wall. Optimal angiographic result was achieved with the deployment of a stent. All patients were followed-up clinically for 17.1±5/2 months for an adverse cardiac event. **Results:** Balloon angioplasty, temperature measurements and stent implantation were performed in all patients, without complications. The mean ΔT was 0.84±0.54 °C. Seventeen patients suffered from an adverse cardiac event during the follow-up period. Patients with adverse cardiac events had increased ΔT compared to patients without events. (ΔT: 0.58±0.37 °C vs. 1.02±0.42 °C; P<0.001). The risk for an adverse cardiac event was increased in patients with «hot» plaques (odds ratio: 2.01). This difference was mainly attributed to patients with unstable angina. **Conclusion:** During the mid-term follow-up period, adverse cardiac events are more likely to present to patients undergoing percutaneous intervention with unstable plaques, which have increased local temperature. Accordingly, these patients may require additional treatment, in order to stabilize the unstable atherosclerotic plaques and thus improve the mid-term clinical outcome.

1218-86 Chlamydia Pneumoniae and Inflammatory Markers in Acute Coronary Syndrome: 12 Months Outcome

Harish R. Chandra, Nivedita Choudhary, Carol O'Neill, Marcus J. Zervos, Judith Boura, Gerald C. Timmis, William W. O'Neill. *William Beaumont Hospital, Royal Oak, MI*

Background: The role of infection with *Chlamydia Pneumoniae* (CP) and inflammation in coronary artery disease is controversial. There is a paucity of prospective data regarding their significance in populations at high risk for cardiac events.
Method: We conducted a prospective study on 418 consecutive patients (mean age 65 ± 13 yrs, 63% males) with no confounding co-morbidities who presented to a chest pain center between March and June 1999 and were diagnosed with acute coronary syndrome (ACS). Pertinent clinical and laboratory data were obtained at the time of admission. At 12 month the incidence of major adverse cardiac events (MACE) was ascertained (death, MI, and revascularization). Data were analyzed to evaluate the association between MACE at 12 months and baseline systemic markers of inflammation including high sensitivity C-reactive protein (CRP) and IgG titres against CP
Results: 80% of the patients were seropositive to CP (IgG ≥ 1:64). At 12 months there were 116 MACE (28%) which included 35 deaths (8.4%), 21 MI (5%) and 84 revascularization (20%). No association between IgG titres against CP at baseline and MACE was found (p=NS). The baseline inflammatory markers were significantly higher in the MACE group (CRP: 2.45 ± 4.3 vs. 1.39 ± 2.78 mg/dl, p=0.02, fibrinogen: 367 ± 142 vs. 331 ± 114 mg/dl, p=0.02, and leukocyte count: 8.6 ± 3.6 vs. 7.6 ± 2.7 10^9/L, p=0.01). There was also an incremental incidence of MACE with ascending tertiles of CRP (Figure). On multivariate analysis the only predictors of MACE were CRP (p=0.007), leukocyte count (p=0.04) and not having prior bypass surgery (p=0.011).
Conclusion: Elevated systemic inflammatory markers are independent predictors of adverse cardiac events at 12 months following acute coronary syndrome. Although infection with C. Pneumoniae is endemic in patients with acute coronary syndrome, it is not associated with adverse long term outcome.



1218-87 Plasma Concentrations of Fibrinolytic Factors in the Subacute Phase of Acute Myocardial Infarction Predict Recurrence of Myocardial Infarction

Takeshi Soeki, Yoshiyuki Tamura, Hisanori Shinohara, Yuki Sawada, Nobuo Fukuda. *Zentsuji National Hospital, Zentsuji, Japan*

Background: The intravascular fibrinolytic system is regulated by a balance between tissue type plasminogen activator (t-PA) and plasminogen activator inhibitor-1 (PAI-1). The prognostic value of these fibrinolytic proteins has also been reported in patients with coronary artery disease. However, the association between recurrent MI and plasma concentrations of fibrinolytic factors during the acute and subacute phases of MI is unknown.
Methods: We recruited 106 patients who survived a confirmed first AMI between 1993 and 1998 in our hospital. From these patients, a total of 94 (72 men and 22 women, mean 66 years) with complete follow-up were included in the present study. The control group for comparison of plasma concentrations of t-PA and PAI-1 consisted of 50 patients who had no coronary artery stenosis. Blood samples were obtained at the time of admission for first acute MI and on the 28th day after admission. Plasma concentrations of t-PA and PAI-1 antigens were measured by enzyme immunoassay. Patients were followed for a mean of 45 months after these measurements, or until March 2000. The primary end points of this study were fatal or nonfatal acute MI. **Results:** Of the 94 patients who were available for follow-up, 6 had recurrent MIs. Both the plasma t-PA and PAI-1 concentrations were elevated on day 1 of acute MI compared to the control group and decreased by day 28, but remained higher than those in the controls. Using a stepwise variable choice model of Cox proportional hazards analysis, only t-PA concentrations in the subacute phase were significant predictors of recurrent MI (relative risk per SD 3.17, p<0.01). We further found that independent of other risk factors, the number of vessels with stenosis, and the use of drugs, an elevated t-PA concentration was predictive of recurrent MI. **Conclusions:** The increase in plasma fibrinolytic factors seen during the acute phase of MI is probably a reaction to thrombus formation, and that seen in the subacute phase is more likely to be due to dysfunction of vascular endothelial cells, based on progressive atherosclerosis. A rise in endogenous t-PA concentration during the subacute phase of MI can predict the recurrent MI.

1218-88 Minor Myocardial Damage and Prognosis: Are Spontaneous and Percutaneous Coronary Intervention-Related Events Different?

Martijn Akkerhuis, John H. Alexander, Barbara E. Tardiff, Eric Boersma, Robert A. Harrington, Michael Lincoff, Maarten L. Simoons. *Thoraxcenter, University Hospital Rotterdam, Rotterdam, The Netherlands*

Background: The relevance of the adverse prognostic implications of CK-MB elevation after PCI remains controversial. Therefore, we compared the relationship between the level of post-procedural CK-MB elevation and the risk of death after 6-month follow-up with the relationship between the level of CK-MB elevation and mortality in patients with acute coronary syndromes (ACS) without ST-elevation treated medically.
Methods and Results: In the PURSUIT trial, 5583 of 9461 patients with a non-ST-elevation ACS did not undergo PCI or CABG and had at least 1 CK-MB sample collected during index-hospitalization. There was a gradual increase in 6-month mortality with higher CK-MB levels (Table). The prognostic significance of cardiac enzyme elevation after PCI was assessed in a combined analysis using data from the CAPTURE, EPIC, EPILOG, IMPACT-II and PURSUIT trials. This analysis in 8838 patients revealed a direct, proportional relation between post-procedural (<48h after PCI) CK-MB levels and 6-month mortality (Table).

6-Month mortality by category of peak CK-MB level

	Spontaneous (n=5583)			Post-PCI (n=3255)			P
CK-MB/ULN	n	%	OR (95% CI)	n	%	OR (95% CI)	
0-1	109/2658	4.1		35/1748	1.3		
> 1-3	125/1367	8.6	2.2 (1.7-2.9)	27/1374	2.0	1.5 (1.0-2.4)	0.15
> 3-5	45/498	9.0	2.3 (1.4-3.5)	7/303	2.3	1.8 (0.8-3.9)	0.34
> 5-10	44/311	14.3	3.9 (2.6-5.9)	13/301	4.3	3.4 (1.9-6.2)	0.71
> 10	28/199	13.5	4.3 (2.7-6.9)	25/310	7.4	6.1 (3.8-9.8)	0.23

Odds ratio (OR) for risk relative to risk in category with CK-MB ratio 0-1. P by Breslow-Day test for heterogeneity of OR of post-PCI CK-MB elevation vs. OR of spontaneous CK-MB elevation within each enzyme category.

The 6-month mortality rates were lower after procedure-related compared with spontaneous infarcts. Yet, the relative increase in 6-month mortality with each increase in the category of peak CK-MB level was of the same magnitude as all tests for heterogeneity of the odds ratios were nonsignificant.
Conclusion: The dose-response relationship between the magnitude of post-procedural CK-MB elevation and 6-month mortality, as well as the consistency of this finding among the different studies indicate that peri-procedural myocardial damage is an important marker of adverse outcome.

POSTER SESSION

1219 Novel Diagnostic and Pathological Techniques in Acute Coronary Syndromes

Tuesday, March 20, 2001, Noon-2:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 1:00 p.m.-2:00 p.m.

1219-89 The Temperature of Atherosclerotic Plaques is Correlated With Matrix Metalloproteinases Concentration in Patients With Acute Coronary Syndromes

Konstantinos Toutouzas, Christodoulos Stefanadis, Eleftherios Tsiamis, Manolis Vavuranakis, Costas Tsioufis, Dorothea Tsekoura, Sofia Vaina, Pavlos Toutouzas. *Hippokration Hospital, Athens, Greece*

Background: Acute coronary syndromes are the result of atherosclerotic plaque rapture, which may be enhanced by local secretion of matrix metalloproteinases (MMPs). Thus, an inflammatory process may be involved in plaque rupture. The aim of the present study was to investigate the association between inflammation, as it is estimated by the measurement of MMPs plasma and serum level and the temperature of the atherosclerotic plaques in patients with acute coronary syndroms. **Methods:** We used sandwich enzyme immunoassay and we measured serum MMP-2 and plasma MMP-9 in 15 patients suffering from acute coronary syndromes (10 with acute myocardial infarction and 5 with unstable angina) and in 17 with stable effort angina. A thermography catheter, which was developed in our institution was used, in order to measure temperature difference (ΔT) between the atherosclerotic plaque and the normal wall vessel. **Results:** Patients with acute coronary syndromes had elevated MMP-9 compared to patients with effort angina (table). There was no difference in MMP-2 concentration between the two groups. Patients with acute coronary syndromes had greater ΔT compared to patients with effort angina. A good correlation was detected between MMP-9 concentration and ΔT in patients with acute coronary syndromes ($P<0.05$, $r=0.62$). **Conclusions:** Patients with acute coronary syndromes had increased concentration of plasma MMP-9, which was well correlated with ΔT. This finding suggests, that plaque rupture may be due to an inflammatory process, leading to increased temperature of the culprit atherosclerotic plaques.

	ACS	EA	P Value
ΔT (°C)	0.85 +- 0.5	0.12 +- 0.1	< 0.03
MMP-9 (ng/ml)	16.1 +- 12.3	10.4 +- 6.4	< 0.05
MMP-2 (ng/ml)	391.7 +- 95.5	378.4 +- 77.7	NS

1219-90 Identification of Lipid-Rich Plaques in Human Coronary Artery Autopsy Specimens by Near-Infrared Spectroscopy

Pedro R. Moreno, S. Eric Ryan, David Hopkins, Barry Wise, K-Raman Purushothaman, William E. Charash, William O'Connor, James E. Muller. *Gill Heart Institute, University of Kentucky, Lexington, KY, InfraReDx, Inc, Cambridge, MA*

Background: A method is needed to identify non-stenotic, lipid-rich coronary plaques that are likely to cause acute coronary events. Near-infrared spectroscopy (NIRS) can provide information on the chemical composition of tissue, and could be adapted for vulnerable plaque identification in living patients. **Methods:** We tested the ability of NIRS to identify lipid-rich coronary plaques in 146 arterial sections from 14 cadaver hearts. Sections were scanned using the fiber optic probe of the NIRSystems 6500 instrument. Reflectance spectra were measured over the range from 400 to 2500 nm (visible and NIR light). After scanning, sections were processed with elastic trichrome stain. Lipid areas were identified by light microscopy, and quantified by computerized planimetry (Zedex system). The 146 sections were divided into a training set of 70 sections for algorithm development, and a test set of 76 sections. Two chemometricians (DH, BW), each using a separate method, performed predictive analysis in the test set, while blinded to the histologic results. **Results:** Lipid areas varied from 0.07 to 2.0 mm2, with a mean of 0.58 mm2. The chemometric partial least square (PLS) model detected lipid areas above or below 0.6 mm2 with 83% sensitivity and 94% specificity (Table). A different approach (PLS-DA model) detected sections with lipid areas above and below 0.07 mm2 with 95% sensitivity and 96% specificity (Table). **Conclusion:** Near infrared spectroscopy can classify human coronary plaques according to their lipid content, the primary determinant of vulnerability. These findings support efforts to develop a NIRS catheter system to detect vulnerable coronary plaques in living patients.

PLS Model	NIR (+)	NIR (-)	PLS-DA Model	NIR (+)	NIR (-)
Lipid > 0.6 mm2	5	1	Lipid (+)	21	1
Lipid < 0.6 mm2	4	60	Lipid (-)	2	46

1219-91 Myocardial Reperfusion With Intravenous Myocardial Contrast Echocardiography in Patients With Optimal Coronary Recanalization (TIMI 3 Flow) After Acute Myocardial Infarction

Paolo Colonna, Massimo Ruscazio, Roberta Montisci, Christian Cadeddu, Giorgio Lai, Mauro Cadeddu, Raimondo Pirisi, Luigi Meloni, Sabino Iliceto. *Department of Cardiovascular and Neurological Sciences , University of Cagliari, Cagliari, Italy*

Background: Myocardial contrast echocardiography is capable to identify coronary microvascular reperfusion in patients after acute myocardial infarction. We hypothesized that microvascular reperfusion is superior to TIMI flow grade in predicting myocardial viability and left ventricle functional recovery in patients with acute myocardial infarction. **Methods:** We studied 55 patients (mean age 59.8±7.4) with acute myocardial infarction (20 anterior, 8 lateral and 27 inferior) with intravenous myocardial contrast echocardiography using power Doppler in intermitting mode during injection of Levovist. A patient was considered as having adequate reflow if ≥50% of segments within the risk area was fully opacified. A dobutamine echocardiography was performed 3 days after the acute phase, to evaluate the presence of myocardial viability. According to TIMI grading in the infarcted related artery at catheterization and presence or absence of reflow at intravenous contrast echocardiography, patients were divided into 3 groups: patients with TIMI 0, 1, 2 flow (n=26); patients with no-reflow despite restoration of TIMI 3 flow (TIMI 3 no-reflow group, n=10), patients with reflow after restoration of TIMI3 flow (TIMI 3 reflow group, n=19). **Results:**

Results		TIMI 0,1,2	TIMI 3 No reflow	TIMI 3 Reflow
No-reflow ratio (%)		57.9±35.4	60.4±12.5	17.3±20.4*
Risk area wall motion score index	in the first day	2.7±0.3	2.7±0.3	2.6±0.3
	At dobutamine	2.2±0.6‡	2.1±0.4‡	1.5±0.5*‡
	After 3 months	2.2±0.6‡	2.1±0.2‡	1.4±0.6*‡
Global wall motion score index	in the first day	1.7±0.3	1.7±0.3	1.8±0.3
	At dobutamine	1.6±0.4	1.6±0.2	1.3±0.3†‡
	After 3 months	1.6±0.4	1.6±0.2	1.3±0.4†‡

* $p<0.001$ and † $p<0.05$ vs TIMI 0,1,2 and TIMI 3 No-reflow patients; ‡ $p<0.001$ vs same group in the first day.

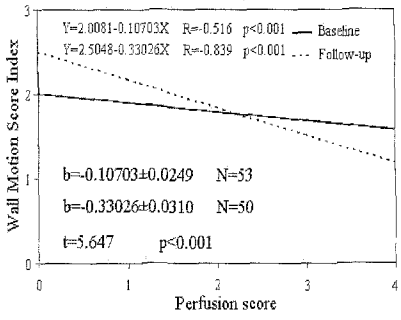
Conclusions: In patients with acute myocardial infarction and optimal angiographic recanalization (TIMI3), the preserved microvasculature at contrast echocardiography is strongly related to viable myocardium and functional recovery. Patients with no-reflow at contrast echocardiography, despite a coronary recanalization with a TIMI 3 flow grade, behave similarly to patients with a bad or absent coronary recanalization.

1219-92 Reperfusion Imaging in Anterior Myocardial Infarction. The Open Perforator Hypothesis

Paolo Voci, Enrica Mariano, Francesco Pizzuto, Francesco Monti, Gianluca Plaustro, Giovanni Testa, Mario Cardini, Paolo E. Puddu. *Section of Cardiology II University of Rome "La Sapienza", Rome, Italy, "Celio" Military Hospital, Rome, Italy*

Background. The TIMI flow scale may not reflect the adequacy of myocardial reperfusion after myocardial infarction (MI). High-resolution transthoracic color-Doppler allows to image the left anterior descending coronary artery (LAD) and its perforating branches in anterior MI. We have assessed the impact of open LAD and perforators on recovery of left ventricular function after MI. **Methods.** We have studied 53 unselected patients (40 M, 13 F, age 63±13 years, weight 76±12 kg) with anterior MI, undergoing thrombolysis (24 pts), primary LAD stenting (18 pts) or none (11 pts). Reperfusion imaging was performed by a 7MHz probe, connected to an Acuson Sequoia C256 ultrasound unit. The mid-distal tract of the LAD and perforators in 4 segments of the anterior apical wall (mid anterior, apical anterior, apical lateral, septal lateral) were imaged. Reperfusion score was: 1: LAD closed, no perforators; 2: LAD open, no perforators; 3: LAD open 1-2 segments with perforators; 4: LAD open, 3-4 segments with perforators. Wall motion score index (WMSI), ejection fraction (EF), end-diastolic volume index (EDVI) and end-systolic volume index (ESVI) were measured at baseline and 3 months follow-up (50 pts). Coronary angiography was used to assess TIMI flow. The linear regression method was used to describe the relationship between perfusion score and WMSI, EF, EDVI, ESVI. **Results.** The sensitivity of color-Doppler to detect LAD patency was 97.8%, specificity 83% and diagnostic accuracy 96.1%. There was a significant correlation between perfusion score at baseline and recovery of WMSI at follow-up, with an intersect corresponding to perfusion score 2 (Figure). Perfusion score also predicted EF, EDVI and ESVI at

follow-up, better than TIMI flow. **Conclusions.** Noninvasive coronary Doppler allows to assess LAD patency after MI. Perforators are landmark of myocardial viability, and may reflect the adequacy of myocardial reperfusion.



1219-93 Coronary Flow Velocity Reserve as a Predictor of Left Ventricular Volume and Functional Change After Acute Myocardial Infarction

Seung-Jea Tahk, Myeong-Ho Yoon, Joon-Han Shin, Zhe-Xun Lian, So-Yeon Choi, Hyuk-Jae Chang, Han-Soo Kim, Byung-il W. Choi. *Ajou University, Suwon, South Korea*

Background: It has been known that coronary flow velocity reserve (CFR) represents the degree of microvascular integrity. This study was designed to evaluate the value of CFR in the prediction of left ventricular volume and functional change after acute myocardial infarction (AMI). **Methods:** To avoid the effect of epicardial stenosis on CFR, intracoronary adenosine-induced CFR of infarct-related artery (IRA) was measured by Doppler wire after successful elective angioplasty or stenting (diameter stenosis<30% and TIMI flow>2) in 80 AMI patients (67 male, mean age: 55±11 years) within 7 days after onset. To evaluate the area of ischemic injury as a whole, CFR was measured at distal segment adjacent to angioplasty site. Left ventricular end diastolic volume index (LVEDVI), ejection fraction (LVEF), and global left ventricular wall motion score index (LVWMSI) were assessed by echocardiography before and after angioplasty (mean: 9±7 months). Receiver operating curve of CFR were used to determine the accuracy (area under curve: AUC) and best cut-off value (BCV) in relation to LV volume and functional change. **Results:** Mean CFR was 1.88±0.58. In relation to the prediction of LVEDVI and LVWMSI change, accuracy was 83.1% on the BCV of 1.7, and 66.8% on the BCV of 1.3, respectively. Patients were divided into 3 groups according to the level of CFR. LVEDVI, LVEF, and LVWMSI changes between baseline and follow-up were compared. Patients with CFR>1.7 showed significant decrease in LVEDVI with improvement in LVEF and LVWMSI. Patients with CFR 1.3-1.7 showed significant increase in LVEDVI with improvement in LVEF and LVWMSI. Patients with CFR<1.3 showed significant increase in LVEDVI without improvement in LVEF and LVWMSI (table).

	Baseline			Follow-Up		
	LVEDVI	LVEF	LVWMSI	LVEDVI	LVEF	LVWMSI
CFR>1.7(n=39)	45±17	52±9	1.49±0.28	38±14*	61±9*	1.22±0.22*
CFR 1.3-1.7(n=32)	44±17	47±8	1.64±0.26	48±14*	55±10*	1.40±0.31*
CFR<1.3(n=9)	48±21	43±9	1.72±0.30	68±24*	43±10	1.73±0.38

* p<0.05 for Baseline vs. Follow-Up **Conclusion:** Coronary flow velocity reserve, measured after relief of epicardial stenosis, may be useful predictor of left ventricular volume and functional change after acute myocardial infarction.

1219-94 Left Ventricular Electro-Mechanical Mapping in Patients Without Previous Myocardial Infarction: Comparison with Stress Perfusion Imaging

Irene Bossi, Glen Van Langenhove, Jean Fajadet, Patrick Serruys, Nicolas Fourquet, Catherine Klersy, Jean Marco. *Clinique Pasteur, Toulouse, France, Thorax Center, Rotterdam, The Netherlands*

Background. The Biosense Noga is a catheter-based system for electro-mechanical mapping of the left ventricle. The combination of linear local shortening (LLS) data as tests of local mechanical function and local intracardiac signals (unipolar voltage = UV) as tests of electrical function provides information about local electromechanical coupling. **Methods.** Linear local shortening and unipolar voltage were measured in 20 patients without previous myocardial infarction, with documented coronary artery disease and reversible defects at stress/redistribution nuclear perfusion imaging. The endocardial sites were divided into 10 anatomic regions and compared with the equivalent segments visualized scintigraphically. Stress nuclear images were analyzed by single photon emission tomography and perfusion defect severity was defined using a semiquantitative scoring of segments (0=normal perfusion, 1=moderate reduction, 2= severe reduction, 3=absent uptake). **Results.** A total of 176 endocardial segments had adequate scintigraphic and Noga data for comparison. The distribution of means ± SD LLS and according to thallium uptake is reported in Table. **Conclusions.** UV correlated significantly with the severity and extent of stress perfusion defects in patients wih no previous MI. UV potentials appears able to identify regions with severe perfusion defects and preserved mechanical function .

	0	1	2	3	p-values
LLS (%)	12.5 ± 7.8	8.28 ± 8.6	9.88 ± 5.9	10.9 ± 4.6	ns
UV (mV)	14.7 ± 5.3	11.9 ± 5.6	13.5 ± 4.7	8.9 ± 5.6	0.0003

POSTER SESSION

1220 Complications of Acute Myocardial Infarction

Tuesday, March 20, 2001, Noon-2:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 1:00 p.m.-2:00 p.m.

1220-95 Effect of Anti Arrhythmic Treatment for Sustained Ventricular Tachycardia in the Setting of Acute Myocardial Infarction

David M. Yamada, Sana M. Al-Khatib, E. Magnus Ohman, Eric J. Topol. *Cleveland Clinic Foundation, Cleveland, OH, Duke University, Durham, NC*

Background: The effect of anti-arrhythmic treatment for sustained ventricular tachycardia (VT) during hospitalization for acute MI remains largely unknown. Amiodarone has demonstrated promise as an acute agent for cardiac arrest and for selected patients following MI. Sotolol is not well studied in acute MI patients, but has properties related to beta blockade that may be cardioprotective. Our purpose was to determine effect of these anti-arrhythmic agents on mortality in this setting. **Methods:** We studied patients enrolled in GUSTO-IIb and GUSTO-III who presented with acute MI and suffered in-hospital sustained VT. Baseline variables and outcomes were analyzed based on administration of anti-arrhythmic agents during hospitalization. **Results:** Of 765 patients, 165 received amiodarone, 474 received anti-arrhythmic treatment not including amiodarone, and 126 were given no anti-arrhythmic drug. Sotolol was used in 33 patients. Those given amiodarone were older, had worse Killip class, and a higher frequency of previous MI compared to the other patients. By univariate analysis, patients receiving amiodarone had a non-significantly higher rate of 30-day death when compared to those given other anti-arrhythmic agents (36.4% vs 27.8%, p=.13) and those given no anti-arrhythmic drug (36.4% vs 28.6%, p=.35). In a Cox proportional hazards analysis, amiodarone administration was associated with a non-significantly lower rate of 30-day death (hazard ratio (HR)=0.72, 95% CI=0.46- 1.1, p=0.14) and one-year death (HR=0.81, 95% CI .54-1.2, p=0.28). Although sotolol was used infrequently (N=33), its use was associated with lower 30-day mortality when compared to other medications (6.1% vs 31.4%, p=0.001) and no medications (6.1% vs 28.6%, p=0.006). **Conclusions:** In the setting of sustained VT during hospitalization for acute MI, amiodarone treatment is not strongly associated with improved survival. Sotolol may improve prognosis. Prospective randomized trials should be undertaken.

1220-96 Advanced Age Impairs Development of Collateral Vessels to Infarct Related Artery in Patients With Acute Myocardial Infarction

Toshiya Kurotobi, Hiroshi Sato, Hideyuki Sato, Issei Shiotani, Eiji Hishida, Kunihiro Kingjoe, Daisaku Nakatani, Atsushi Hirayama, Tsunehiko Kuzuya, Kazuhisa Kodama, Masatsugu Hori. *Osaka University Graduate School of Medicine, Suita, Japan, Osaka Police Hospital, Osaka, Japan*

Background: Animal experiments have shown that advanced age blunts angiogenesis and development of new vessels in response to angiogenic cytokines. We investigated the hypothesis that development of collateral vessels (Coll) to infarct related artery (IRA) is impaired with aging in patients with acute myocardial infarction (AMI). **Methods:** Of consecutive 1360 patients with AMI, 622 patients who fulfilled the following criteria were enrolled in this study : 1) Coronary angiograms were obtained within 72 hrs after the onset of AMI, and 2) IRA showed complete occlusion (TIMI grade 0 or 1). Coll to IRA was evaluated according to the Rentrop score. The grades from 1 to 3 were defined as significant Coll. In random selected 50 patients, vascular endothelial growth factor (VEGF) and hepatic growth factor (HGF) were measured at chronic phase. **Results:** Prevalence of Coll significantly decreased with advanced age (45.6% in <50 y.o., 44.6% in 50-59 y.o., 42.6% in 60-69 y.o., 32.0% in >70 y.o., p<0.05), and advanced age was an independent predicting factor to decrease collateral development to IRA (odds ratio 1.02, 95% 1.01-1.03, p<0.05). Serum VEGF and HGF level were not significantly different in each decade. Pre-infarction angina significantly increased the prevalence of Coll development below 70 y.o. (48.5% vs. 39.5%, p<0.05), but this effect was impaired above 70 y.o. (33.9% vs. 31.5%, n.s.). Multivariate analysis showed that the absence of Coll was an independent predictor of in-hospital mortality in elderly patients above 70 y.o. (odds ratio 5.8, 95% 1.2-26.8), although this effect was not observed in patients below 70 y.o. (odds ratio 1.7, 95% 0.4-7.7). **Conclusion:** Advanced age may blunt development of Coll to IRA in patients with AMI due to lack of response against coll promoting stimuli. This abnormality may contribute to poor prognosis in elderly patients with AMI.

1220-97 Angiographic Findings in Non Q vs. Q wave Myocardial Infarction After Thrombolysis for ST Segment Elevation Infarction. Results From the DANAMI Trial

Peter Clemmensen, Peer Grande, Jan K. Madsen, Walter B. Nielsen, Galen S. Wagner, Kari Saunamäki, Eli Kassis, Per Thayssen, Klaus Rasmussen, Torsten T. Nielsen, Torben Haghfelt, Stig Haunsoe. *The Heart Center, Rigshospitalet, Copenhagen, Denmark*

Background. Acute myocardial infarction (AMI) is often classified as Q or non-Q wave based on the ECG morphology. Although non-Q wave AMI are smaller the prognostic implicationsand need for invasive study remains controversial. **Methods.** 1008 patients with inducible ischemia after being treated with thrombolysis for ST-segment elevation AMI were randomized in the DANAMI trial to conservative treatment or invasive evalua-

tion. For the present substudy the patients were classified as Q wave or non-Q AMI, and the analysis limited to those in the invasive arm, with complete angiographic assessments (483 / 503 patients). **Results.** The loyalty to the randomization was the highest ever reported in a trial of invasive vs. conservative treatment. At 2 months revascularizations had been performed in 83% randomized to an invasive strategy and only 1.5% in those randomized to conservative treatment. As previously reported, the invasive strategy was associated with a more favorable outcome but the largest relative reduction in the combined end-point (death, re-infarction, and readmissions with unstable angina) was attained among patients with non-Q wave AMI (RR 43% vs. RR 32%; difference= 11%; 95% Confidence Interval: 8.6-14.0%, 0.023). The table demonstrate the cardiac catheterization findings in patients with non-Q and Q wave AMI. "Normal coronaries" was defined as <50% stenosis. **Conclusions.** Non-Q AMI evolving after ST-segment elevation AMI treated with thrombolytic therapy is associated with more preserved LVEF. Despite inducible ischemia prior to discharge "normal" coronary arteries is a common finding in non-Q AMI patients, but these patients also have a higher incidence of left main stem stenosis and should be offered invasive evaluation to the same extent as Q-wave AMI patients.

Cardiac catheterization finding in patients with non-Q and Q wave AMI

N	Non-Q 132	Q wave 351	p value
Normale coronaries (%)	21 (15.9)	18 (5.1)	0.0001
1 vessel disease (%)	50 (37.9)	187 (53.3)	0.0035
2 vessel disease (%)	27 (20.5)	66 (18.8)	NS
3 vessel disease (%)	24 (18.2)	65 (18.5)	NS
Left main stem (%)	10 (7.6)	15 (4.3)	0.075
LVEF (%)	62 (55-70)	56 (47-64)	0.00001

1220-98 Hospital Outcomes in Patients Presenting With Congetive Heart Failure Complicating Acute Myocardial Infarction

Audrey H. Wu, Lori Parsons, Nathan R. Every, Eric Bates. *University of Washington, Seattle, WA, University of Michigan, Ann Arbor, MI*

Background: The impact of congestive heart failure (CHF) in the setting of acute myocardial infarction (AMI) on hospital outcomes is not established.
Methods: The National Registry of Myocardial Infarction 2 database was analyzed to determine hospital outcomes for thrombolytic-eligible patients admitted with CHF (Killip class II or III) complicating AMI.
Results: A total of 190,518 patients were identified (36,303 with CHF). Patients presenting in CHF were older (72.6±12.5 vs. 63.2±13.5 yrs.), had a longer time from symptom onset to hospital presentation (2.80±2.6 vs. 2.50±2.4 hrs.), and had a higher prevalence of anterior/septal AMI (38.8% vs. 33.3%), diabetes (33.1% vs. 19.5%), and hypertension (54.6% vs. 46.1%) (all p<0.00005). Patients with CHF were more likely to receive ACE inhibitors, but those without CHF were more likely to be treated with aspirin, beta-blockers, thrombolytics or primary angioplasty. Patients presenting in CHF had a longer length of stay (8.1±7.1 vs. 6.8±5.3 days, p<0.00005) and greater risk for adverse hospital outcomes. CHF on admission was the strongest predictor of hospital death in multivariate analysis (OR 1.69; 95%CI 1.62, 1.75).

Treatment /outcome	N	No CHF (%)	CHF (%)	P
Aspirin	164,695	89.0	75.7	<0.00005
ACE inhibitor	29,213	13.0	25.4	<0.00005
Oral beta blocker	74,080	41.7	27.0	<0.00005
Thrombolytic	101,581	58.0	33.4	<0.00005
Primary PTCA	25,596	14.6	8.6	<0.00005
Recurrent AMI	5,182	2.7	3.0	0.002
Cardiogenic shock	10,604	3.9	12.6	<0.00005
Cardiac arrest	9,783	4.4	8.3	<0.00005
Hospital death	18,839	7.2	21.4	<0.00005

Conclusion: Patients with CHF complicating AMI have more medical comorbidities and anterior/septal AMI at presentation, and are at higher risk for hospital mortality and adverse outcomes. Despite this, they are less likely to be treated with aggressive reperfusion strategies and some medications with proven mortality benefit.

1220-99 Reperfusion Induced Bradycardia and Hypotension Is Common With Proximal but Not Distal Acute RCA Occlusions: Role of the Ischemic Right Ventricle

Daniel T. Lee, Vinh D. Nguyen, William W. Oneill, James A. Goldstein. *William Beaumont Hospital, Royal Oak, MI*

Background: Reperfusion of the acutely occluded right coronary artery (RCA) may result in abrupt bradycardia and hypotension, which has been attributed to stimulation of Bezold-Jarisch reflexes arising from the ischemic left ventricle (LV). Based on clinical observations in patients with RV infarction from our group and others suggesting that bradycardia and hypotension commonly occurs following reperfusion of proximal RCA occlusions, we hypothesized that reflexes arising from the ischemic RV may play a role.
Methods: We retrospectively analyzed the incidence of reperfusion induced bradycardia and/or hypotension in patients with acute inferior myocardial infarction undergoing primary angioplasty of RCA lesions proximal to the RV branches (n = 144) or distal to the RV branches but before the LV branches (n =51).
Results: Reperfusion of proximal RCA occlusions resulted in abrupt hypotension in 62 (43%) patients and bradycardia in 54 (38%) patients. In contrast, reperfusion of distal RCA occlusions rarely resulted in hypotension (6%, p < 0.001 vs proximal) or bradycardia (10%, p < 0.001 vs proximal).
Conclusion: These data demonstrate that reperfusion-induced bradycardia and hypotension commonly occur in patients with proximal RCA occlusions affecting the RV and LV, but rarely occurs with distal occlusions supplying the LV alone. These findings suggest that reperfusion induced reflexes arising from the ischemic RV may play a role in abrupt bradycardia and hypotension.

1220-100 US and Non US Outcomes Are Similar for Patients With Cardiogenic Shock: A Report From the SHOCK Trial

Venu Menon, Jacques Col, Lynn A. Sleeper, Mark Menegus, Christopher E. Buller, John French, Mark Porway, Harvey D. White, John G. Webb, Jean Boland, Philip Aylward, Judith S. Hochman. *St. Luke's-Roosevelt Hospital Center, New York, NY*

Background: Superior outcomes for US compared to non-US patients with cardiogenic shock(CS) in both GUSTO-I and GUSTO-III megatrials have been previously reported. This disparity was hypothesized to be due to decreased rates of revascularization (PTCA/CABG) and IABP in non US institutions. If outcome following CS is determined by rates of revascularization, then analysis of the early revascularization (ERV) arm of the randomized SHOCK trial which was protocol mandated should result in US/non-US outcomes being similar. **Methods:** Outcomes in US (n=89) vs. non-US patients (n=63) randomized to ERV were compared. Protocol mandated PTCA/CABG was performed as indicated in both groups within 6 hours of randomization and 18 hours of shock. **Results:**US and nonUS patients were similar with respect to age, gender, prior diabetes, prior MI, and PCWP (all p > 0.10). There was a greater h/o prior HTN amongst US patients (58 vs. 36%, p=0.012)and time from MI to CS tended to be longer (p =0.061).

US vs. non-US

Variable	US (n=89)	non-US (n=63)	p-value
Revascularization Rate	85%	89%	0.630
IABP Rate	85%	89%	0.630
30-day Mortality Rate	44%	51%	0.414

By protocol, rates of revascularization and IABP use were similar at both US and non-US sites. No difference in 30-day mortality rates based on geographic location were observed. Crude OR and Adjusted OR(adjusted for prior hypertension and time from MI to CS) for death amongst non US patients was 1.32 (95% CI 0.69,2.53) and 1.44 (95% CI 0.73, 2.89, p= 0.299) respectively. **Conclusion:** The SHOCK trial demonstrated similar rates of revascularization and IABP utilization and similar mortality for US and non-US patients. Although limited by small numbers and wide confidence intervals, our observations suggest therefore that worldwide outcome following cardiogenic shock is similar when a uniform treatment strategy is adopted.

ORAL CONTRIBUTIONS

863 Evolving Parameters of Risk and Quality of Life After Acute Coronary Syndromes

Tuesday, March 20, 2001, 2:00 p.m.-3:30 p.m.
Orange County Convention Center, Valencia D

2:00 p.m.

863-1 What Is an MI? Prospective Analysis of the Diagnostic and Prognostic Impact of Adding Troponins to the Definition of Myocardial Infarction

Shaun Goodman, Jeanna Johnson, Cynthia Sullivan, Ph Gabriel Steg, Kim Eagle, Keith A. A. Fox, Jose Lopez-Sendon, Gilles Montalescot, Andrzej Budaj, Brian Kennelly, Joel Gore, for the GRACE Investigators. *Canadian Heart Research Centre, Toronto, ON, Canada, Division of Cardiovascular Medicine, University of Massachusetts Medical School, Worcester, MA*

Background: The new consensus of The Joint ESC/ACC Committee for the Redefinition of Myocardial Infarction suggests that any amount of myocardial necrosis caused by ischemia should be labelled as an infarct. This is in part based upon data derived from either selected clinical trial populations or retrospective analyses linking troponins with worse prognosis. The resulting increase in the sensitivity of defining criteria for myocardial infarction with the use of troponins could have a substantial impact on the worldwide incidence of myocardial infarction. Further, the prognostic value of this new definition has not been evaluated prospectively in a large, unselected population of patients with acute coronary syndromes (ACS).
Methods: We examined the myocardial infarction rates and prognostic value of peak standard (CK, CK-MB) and new (troponin I/T) cardiac markers in 3,420 of 8,213 ACS patients with both measurements enrolled in the Global Registry of Acute Coronary Events (April 1999-June 2000). GRACE is a prospective, multinational, observational study of patients hospitalized with ACS in 94 centers in 15 countries from 4 continents, including Europe and the Americas.

Results: The addition of isolated troponin positive (Tn+) patients resulted in a further 15%, 26%, and 9% increase in the rate of myocardial infarction diagnosis beyond the utilization of either CK ≥ upper limit of normal (ULN), CK ≥ 2 times (2x) ULN, or CK-MB ≥ ULN, respectively. The odds ratio (OR) for in-hospital mortality was significantly* higher in troponin-positive patients (see Table).

	CK <= 2X ULN, Tn-	CK <= 2X ULN, Tn+	CK > 2X ULN, Tn-	CK > 2X ULN, Tn+
n(%)	1,285 (38%)	900 (26%)	124 (4%)	1,111 (32%)
OR (95% CI) for in-hospital death	1	3.0* (1.6, 5.7)	2.1 (0.6, 7.4)	5.8* (3.3, 10.1)

Conclusions: The addition of troponin positivity leads to as many as 1 in 4 additional ACS patients meeting the criteria for the diagnosis of myocardial infarction. This group of patients experiences a 3-fold increase in short-term mortality when compared to normal enzyme levels and a 1.5-fold increase compared to the traditional cardiac enzyme definition.

2:15 p.m.

863-2 Elevated Plasma Levels of the Plasmin Activation System, but Not of Thrombin Activation System Correlate With the Sonographic Signs of Plaque Instability in Patients With Unstable Angina

Mariann Gyongyosi, Paul Yang, Ali Hassan, Franz Weidinger, Hans Domanovits, Anton Laggner, Dietmar Glogar, Kurt Huber. *Division of Cardiology, University of Vienna Medical Center, Vienna, Austria*

Background: We determined the possible association between the echocardiographic signs of plaque instability (expansive remodeling, plaque rupture and thrombi) and the increased plasma levels of plasmin and thrombin activation systems in patients with unstable angina. **Methods:** The basal plasma levels of the thrombin activation system (thrombin-antithrombin complex, homocystein, tissue factor pathway inhibitor, and prothrombin fragments 1+2) and the plasmin activation system (tissue-type and urokinase-type plasminogen activator, plasminogen activator inhibitor type-1) were measured in 52 consecutive admitted patients (35 male, 60±12 y) with unstable angina. All patients underwent coronary angiography and intravascular ultrasound 3±2 hours after hospital admission. The atherosclerotic plaque morphology assessed by intravascular ultrasound was determined as plaque composition and eccentricity, plaque disruption, visible thrombi and calcification. Quantitative intravascular ultrasound analyses involved the measurements of lumen, vessel and plaque area of the culprit lesion, proximal and distal reference segments and the types of arterial remodeling. **Results:** Expansive remodeling was associated with significantly larger plasma levels of plasminogen activator inhibitor type-1 (121.6±55 vs 87.7±61.5 and 77.4±42.8 ng/ml, p=0.039) and urokinase plasminogen activator (3.04±1.2 vs 2.15±0.52 and 2.46±0.67 ng/ml, p=0.0263) as compared to constrictive and neutral remodeling. Increased plasma level of urokinase plasminogen activator was associated with plaque rupture (2.95±0.66 vs 2.51±0.87 ng/ml, p=0.0621). Plasma levels of plasminogen activator inhibitor and urokinase plasminogen activator correlated positively with plaque (p=0.0297 and 0.0093) and vessel areas (p=0.010 and p=0.0002). There was no correlation between the plasma levels of thrombin activation system and qualitative and quantitative plaque morphology. **Conclusion:** Elevated levels of parameters of the plasmin activation system, but not the increased levels of thrombin activation system are associated with signs of plaque instability of the culprit lesion in patients with unstable angina.

2:30 p.m.

863-3 Cardiac Enzyme Elevations After Coronary Artery Bypass Grafting Associated With Increased Risk of Death: Results From PARAGON-B

Kenneth W. Mahaffey, Matthew T. Roe, Rodney Sparapani, Christopher B. Dyke, John H. Alexander, Lisa G. Berdan, Christopher B. Granger, Magnus Ohman, Robert M. Califf, Eric J. Topol, Robert A. Harrington. *Duke Clinical Research Institute, Durham, NC*

Background: The clinical importance of cardiac enzyme elevations following coronary artery bypass grafting (CABG) is controversial.

Methods: To evaluate the association between creatine kinase-MB (CKMB) enzyme elevations following CABG and clinical outcomes, we analyzed patients from the PARAGON-B trial that evaluated the glycoprotein IIb/IIIa inhibitor, lamifiban, in patients with non-ST-segment elevation acute coronary syndromes.

Results: A total of 5,225 patients were enrolled of which 790 underwent CABG a median (25^{th}, 75^{th}) 5.9 (2.9, 10.2) days after enrollment. Enzyme data following CABG were available for 390 (49%) of CABG patients. Enzyme elevations were analyzed as a ratio of the peak CKMB and the laboratory upper limit of normal (ULN). Clinical outcomes occurring after CABG in-hospital, at 30 days, and at 6 months stratified by ratio of CKMB elevation are shown:

	MB ≤ ULN	MB 1-3 x ULN	MB 3-5 x ULN	MB 5-10 x ULN	MB ≥ 10 x ULN
N	56	131	66	74	63
In-hospital					
Cardiac Arresi	3.6%	1.5%	0%	2.7%	14.3%
Shock	1.8%	1.0%	0%	4.1%	12.7%
30-day					
Death	3.6%	1.0%	0%	2.7%	14.3%
Stroke	7.1%	3.8%	6.2%	0%	7.9%
6-month					
Death	3.8%	2.3%	0%	4.1%	14.3%

Conclusions: CKMB elevations following CABG are associated with increased risk of adverse in-hospital and long term outcomes. The degree of risk is proportional to the rise in CKMB with a clear excess of shock, cardiac arrest and mortality with CKMB ≥ 10x ULN (p < 0.0001). Other factors may be important and confirmation in larger patient populations is needed.

2:45 p.m.

863-4 Revacularization in Patients With Unstable Coronary Artery Disease: is There Still a Need For CABG?

Elisabeth Stahle, Odd Geiran, Bo Lagerqvist, Hans Pilegaard, Rolf Svedjeholm, Eva Swahn, Lars Wallentin. *Dept Thoracic and Cardiovascular Surgery, University hospital, Uppsala, Sweden, Dept Cardiology, University hospital, Uppsala, Sweden*

Objective: In the FRISCII-study an early invasive strategy reduced the risk for death after 12 months by 44 % in patients with unstable angina as compared to a selective approach with invasive procedures only if indicated by symptoms or severe ischemia at excersice testing. A crucial question was whether early surgery could be accomplished without increased risk of mortality as compared to PCI with treatment only of the suspect culprit lesion. **Methods:** 2,457 patients with unstable angina were randomised to an invasive strategy (n=1,222) or to a non-invasive approach (n=1,235). After 6 months 953 patients (78%) in the invasive group were revascularized, 431 with CABG and the remaining 522 with PCI. In this presentation early mortality in the early invaisve group were analyzed. **Results:** Out of the patients undergoing CABG in the invasive group 8 % had insulin-treated diabetic disease, 4 % had treated heart failure, 7 % had peripheral artery disease, 48 % were 70 yrs or older and 70 % had 3-vessel disease. Comparable figures for those who had PCI were 4 %, 1 %, 4 %, 29 % and 9 %, respectively. If high-risk patients were defined as those having either of these criterias 86 % of the CABG patients were allocated to that group versus 39 % of the PCI patients, 16 % of the high-risk patients had no revascularisation. Overall mortality within 30 days was 1.6 %; 0.4 % for the low-risk group and 2.5 % for high-risk patients. 1.9 % for the CABG patients, 0.2% for the PCI patients and 3.6 % for those who had no intervention. Female sex [odds ratio 5.0] and diabetes [odds ratio 4.2] were independent risk factors for early mortality in patients who underwent CABG. **Conclusion:** The FRISCII trial is to date the only randomised trial that has shown a significant and maintained mortality reduction accomplished with early revascularisation and preceded with antithrombotic treatment in patients with unstable coronary disease. In this trial the vast majority of high risk patients underwent CABG with very low mortality. The study confirm that complete revascularisation with early surgery can be achieved with very low mortality. It can thus be concluded that there is a need for early CABG in patients with unstable coronary syndromes.

3:00 p.m.

863-5 A Comparison of the Impact of Practice Patterns on the Outcomes of Patients With Acute Coronary Syndromes in the USA and Canada: Post Hoc Analysis of ESSENCE and TIMI 11B

Wayne B. Batchelor, David Radley, Marc Cohen, Alexander G. G. Turpie, Anatoly Langer, Shaun Goodman. *Terrence Donnelly Heart Center, Ontario, Canada*

Background Several studies have compared the U.S. and Canada for differences in health care delivery and outcomes in patients presenting with ST elevation MI. The TIMI-III registry focussed on non-ST elevation acute coronary syndromes, and showed higher rates of death, myocardial infarction (MI) or recurrent ischemia in US patients at 6 weeks (18.4% vs Canada 13.9%, p=0.004). However, these results may not reflect contemporary practice patterns for a broad range of hospitals in each country.

Methods We compared the practice patterns and long-term outcomes between 1522 US and 2001 Canadian patients presenting with non ST-segment acute coronary syndromes (unstable angina and non-Q wave myocardial infarction) in the ESSENCE and TIMI 11B studies.

Results Most baseline characteristics, including age (64% vs. 64%), male gender (64% vs 63%), prior MI, aspirin (97% vs. 97%) and beta-blocker use (70% vs. 70%) were similar in the two groups. Baseline TIMI risk scores were also comparable. Obesity (59% vs. 51%) and non-caucasian race (24% vs 7.4%) were more common in the U.S. The cumulative frequency of the composite endpoint of death/MI/urgent revascularization and revascularization procedures are shown in Table 1.

Table 1

	Canada (n=2001)	USA (n=1522)	Log Rank p value
3 Month	n (%)	n (%)	
Death/MI/Urg Revasc	366 (18.5)	278 (18.6)	0.74
Death/MI	176 (8.9)	135 (9.1)	0.78
Any revasc	606 (31.0)	611 (40.8)	<0.001
CABG	272 (14.0)	267 (17.9)	<0.001
6 Month	n (%)	n (%)	p value
Death/MI/Urg Revasc	407 (20.6)	306 (20.6)	0.79
Death/MI	206 (10.5)	152 (10.3)	0.99
Any revasc	663 (34.1)	622 (41.6)	<0.001
CABG	312 (16.1)	281 (19.0)	0.0019
12 Month	n (%)	n (%)	p value
Death/MI/Urg Revasc	459 (23.3)	357 (24.4)	0.39
Death/MI	249 (12.7)	186 (12.8)	0.85
Any revasc	703 (36.3)	644 (43.3)	<0.001
CABG	352 (18.3)	294 (20.0)	0.02

Conclusions In the largest US-Canadian comparative study of acute coronary syndrome outcomes to date, despite the more frequent use of revascularization procedures in the US, long-term clinical outcomes are similar to those observed in Canada.

3:15 p.m.

863-6 **Quality of Life One Year After Invasive Intervention in Unstable Coronary Artery Disease: Results From the FRISC II Invasive Trial**

Magnus Janzon, Lars-Åke Levin, Eva Swahn, FRISC II Investigators. *Institution of Medicine and Care, Linköping University, Linköping, Sweden, CMT, Center for Medical Technology Assessment, Linköping University, Linköping, Sweden*

Background: Both early invasive and non-invasive treatment strategies in patients presenting with unstable coronary artery disease have been used during the acute phase of the disease. Until today there is no published study analysing the quality of life in this important and large patient group in the long-term follow-up. The aim of this study was to identify differences in quality of life between the two treatment groups.
Methods: A total of 2 457 patients, median age 66 years and 70 % men, with unstable angina or non-Q-wave myocardial infarction were randomised to early invasive or non-invasive treatment. The quality of life was measured with the generic quality of life instrument SF 36 (Short Form 36 Health Survey) at time for randomisation, outpatient visits at 3 and 6 months. At one-year follow-up SF-36 was measured in a subgroup of 620 patients. SF-36 is presented in eight scales (range 0-100, where 100 corresponds to full health).
Results: In the FRISC II trial the invasive treatment showed a significant reduction in mortality (2.2 % vs. 3.9 %, p=0.016). At time for randomisation there was no significant differences in quality of life between the groups in six of the scales. At 3 and 6 months follow-up it was a significant difference (p<0.01 in all eight scales) in quality of life favouring the invasive group. The differences still remained significant at one-year follow-up in six of the scales.
Conclusions: Patients with unstable coronary artery disease treated with early invasive strategy have better quality of life measured with SF-36 up to one-year follow-up compared to patients treated with non-invasive strategy.

POSTER SESSION

1249 Outcome Predictors in Acute Myocardial Infarction

Tuesday, March 20, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 4:00 p.m.-5:00 p.m.

1249-75 **Primary Angioplasty in Acute Myocardial Infarction: Does Age Matter?**

Carol Regueiro, Alison Hart, Linda Crawshaw, Shelly McCormick, Michael Anshelevich, Terry Hentosz, Richard Shannon. *Allegheny General Hospital, Pittsburgh, PA*

Background: Recent data suggest that there are substantial variations in the treatment of acute myocardial infarction (AMI) based on age, race, gender and socioeconomic status. Advanced age is associated with graver outcomes in AMI that may benefit from acute coronary interventions. We evaluated the use of primary angioplasty (PA) in AMI in elderly patients treated in an academic referral center. **Methods:** We reviewed the records of a convenience sample of 168 patients with AMI from 1997-2000. Our primary outcome was PA in AMI, defined as coronary intervention within the first 24 hours of admission. Secondary outcomes included use of post-AMI therapies such as Aspirin (ASA), beta-blockers (BB), angiotensin converting enzyme inhibitors, and other anticoagulants (AC). We collected variables including demographics, comorbidities, do-not-resuscitate status, physician characteristics, and severity of illness using the ATLAS system. Univariate analysis was performed on the variable of interest as well as all candidate variables. Subsequent logistic regression modeling incorporated all variables significant on univariate analysis. Insignificant variables that were confounded with age were kept in the final model. **Results:** Unadjusted analysis revealed that older patients were significantly less likely to receive both PA for AMI, and post-AMI BB, or AC (all p<.05). Other factors which had a significant negative impact on use of PA included do-not-resuscitate status, increasing acuity of presenting signs and symptoms, severity of illness, and dementia (all p< .05). After adjustment for these potential confounders, increasing age remained inversely associated with both PA (p< .001), and use of standard post-AMI BB or AC (p<.05). **Conclusions:** Our results indicate differences in the use of both PA and post-AMI therapies in the elderly AMI patients. These differences are not explained by severity of illness and suggest that interventions and standard therapies may be withheld from those who may benefit most.

1249-76 **Primary Angioplasty in the Elderly: Predictors of Angiographic and Clinical Outcome in the Era of Stents and IIb/IIIa Inhibitors**

Satyendra Giri, Jeffrey A. Hirst, Francis J. Kiernan, Daniel B. Fram, Jeffrey J. Popma, Charles A. Primiano, Joseph Mitchel. *Brigham & Women's Hospital, Boston, MA, Hartford Hospital, Hartford, CT*

Prior studies have suggested that primary angioplasty may be the preferred method of reperfusion in the elderly (>75yr) compared to thrombolytic therapy. Less is known about the impact of stents and IIb/IIIa inhibitors on major adverse clinical outcomes (MACE) in this population.

Method: We prospectively studied 901 patients (01/96 - -5/00) treated with PA <12 hr of symptoms, out of which 170 (19%) were elderly. Two angiographers performed quantitative analysis and prespecified clinical variables were entered in to a dedicated database. Independent risk of old age after adjusting for explanatory variables was quantified by logistic regression modeling for 30 day MACE.
Results: The elderly were more likely to hypertensive (64% vs 42%), women (54% vs 26%) and with prior MI (19% vs 13%) but less likely to be current smoker (29% vs 54%), hyperlipidemic (23% vs 48%) and with family history of premature coronary disease (10% vs 42%) [All p<0.05].
Elderly were more likely to present late (325±115 vs 278±88 minutes), in cardiogenic shock (24% vs 12%), three vessel disease (55% vs 30%), fail to achieve TIMI grade 3 flow (15% vs 6%), develop persistent no reflow (13% vs 4%) and have higher 30-day MACE (22.4% vs 13.1%) [All p<0.05].
All clinical and angiographic variables significant (p<0.05) in univariate analysis were included in a forward stepwise logistic regression model. In this model, cardiogenic shock, prolonged symptom-to-balloon time, a final TIMI flow of <3, use of abciximab and higher acute luminal gain were independent predictors of 30-day MACE.
Conclusion: Elderly patients suffer increase MACE compared to young. Prolonged ischemia time and cardiogenic shock at presentation increase the risk of MACE. Because of the protective effect, use of glycoprotein IIb/IIIa inhibitors and larger luminal gain should be advocated in the elderly.

Logistic regression model

Multivariate predictors	Odds Ratio	95% CI Lower	Upper
Cardiogenic shock	4.425	2.616	7.484
Symptom onset to balloon time	1.006	1.004	1.009
Final TIMI grade flow <3	4.865	2.516	9.411
abciximab use	0.449	0.279	0.723

1249-77 **Early ST-Variability Predicts Thrombi in the Infarct Related Artery. A Report From the ASSENT PLUS ST-Monitoring Substudy**

Per Johanson, Monica Eriksson, Gerd Källström, Gunilla Norman, Jenny Rössberg, Ann-Marie Svensson, Helena Svensson, Mikael Dellborg. *Sahlgrenska University Hospital / Östra, Göteborg, Sweden*

Background: Rapid, complete and sustained reperfusion is the goal when treating an acute myocardial infarction. Continuous ST-monitoring has been shown to accurately evaluate reperfusion and reocclusion. Early dynamic changes in the ST-segment shift has been connected to worse outcome, intermittent reocclusions and a higher thrombogenic activity.
Methods: A total of 214 patients from 11 hospitals were included in the vectorcardiographic substudy of the ASSENT PLUS-trial. Inclusion-criteria were the same as in the ASSENT 2-trial. All patients received alteplase and either heparin or dalteparin. An angiogram was planned on day 4-7. Patients were ST-monitored for 24 hours. ST-trend curves were analysed blindly by two independent observers. During the acute phase, 0-4 hours, an increase in ST-vectormagnitude of 25µV for >= 2 minutes was considered as a significant episode of ST-variability. During hours 4 to 24 the cut-off 50µV was used to define a ST-episode, according to our previous vectorcardiographic definitions. Patients with bundle branch block were excluded. 176 of the patients underwent an angiography, which also was core-lab analysed by two persons.
Results: 33 patients showed a thrombus in the infarct related artery. Patients with a thrombus had a longer total duration of ST-variability during the first 4 hours 28 vs. 17.6 minutes, p=0.009. They also had more, 2.1 vs. 0.25 (p<0.0005), and longer ST-episodes during hours four to twenty-four, 25 vs. 2.4 minutes (p<0.0005). Seven patients had vectorcardiographic signs of reocclusion. Out of these, 6 had a thrombus in their infarct related artery, as compared to 27 out of 169 in patients with no sign of reocclusion, p=0.00001. Vectorcardiographic signs of reocclusion during the first 4 hours predicted occurrence of a thrombus in 100% (3 out of 3 vs. 30 out of 173), p=0.0063.
Conclusion: Vectorcardiographic signs of reocclusion, and small dynamic changes here defined as ST-variability and ST-episodes, predict occurrence of thrombi in the infarct related artery, and may lead to consideration of adjunctive therapeutical steps, such as use of a GP IIb IIIa inhibitor or urgent revascularization.

1249-78 **Direct Infarct Intervention in Women: Is There a Gender Difference in Clinical Outcomes?**

Ambika Bhaskaran, Robert M. Siegel, Barbara Barker, Warren Breisblatt, Charles Jost, Warren Zeitlin, Stephen Cantor, Sheryn Shimamoto, Deborah Frazier, Jennifer Vermillion. *Advanced Cardiac Specialists, Gilbert / Phoenix, AZ*

Background: Female gender is regarded as an independent predictor of mortality following MI. We evaluated our registry data over 5 years (5/95-7/00) on 1,036 consecutive patients (338 female; 698 male) who underwent direct infarct intervention (d-PTCA) within 12 hours of onset of symptoms. **Methods:** We analyzed baseline variables, procedural, in-hospital and 12-month clinical outcomes. Compared to men, women were older (61 vs 66 years; p <0.0001), more frequently diabetic (17% vs 25%; p<0.0001) or hypertensive (46% vs 57%; p=0.005). Men were more frequently smokers (38% vs 31%; p=0.002), had higher rate of prior MI (22% vs 14%; p <0.0001) and prior CABG (12% vs 5%; p=0.001). Women took longer to arrive at the hospital (120 vs 97 minutes; p=0.05) but mean time to open vessel from arrival was similar (13 vs 16 minutes; p=0.08). Both groups had similar baseline angiographic variables and LV function (mean LVEF 42.5%).
Results: Procedural success was comparable (97.8% women, 97.6% men; p=0.31). Acute re-occlusion was more frequent in women (0.7% vs 0; p=0.05) with longer hospital stay (4.1 vs 2.9 days; p<0.0001). In-hospital CABG (2% women vs 1% men) and death (0.3% in both) was similar in both groups. The use of anti-platelet drugs, beta-blockers and ACE-inhibitors was similar in both. At 12-month follow-up, mortality (4.2% women,

3.8% men), target vessel re-PTCA (6.9% women, 6.4% men), CABG (3.4% women, 3.7% men) and event-free survival (84.6% women, 85.8% men) showed no significant difference between both groups (p >0.05). Women showed a significant rise in mean LVEF (9%; p=0.046) unlike men (3%; p=0.90). **Conclusions:** D-PTCA appears to be safe and effective in women. Despite unfavorable baseline comorbidities, procedural success is high and comparable to men. Acute reclosure is higher in women and hospital stay longer. At 1 year follow-up, women demonstrate event-free survival rates similar to men. Our experience reinforces that female gender should not be a contraindication to invasive strategy in acute MI. Women appear to achieve greater gains than men in LV systolic performance, suggesting that aggressive strategies may be particularly warranted, for effective myocardial salvage and improved survival.

1249-101 Creatinine Clearance but Not Serum Creatinine on Admission Predicts Early and Late Death After Primary Angioplasty

Simon R. Dixon, Cindy L. Grines, David A. Cox, Gregg W. Stone, Eulogio Garcia, Luiz A. Mattos, Bruce R. Brodie, Alessandro Giambartolomei, Lorelei L. Grines, Judith A. Boura, William W. O'Neill, Marie-Claude Morice. *William Beaumont Hospital, Royal Oak, MI*

Background: Few data exist regarding the influence of mild or moderate renal dysfunction on early or late outcome after acute myocardial infarction (AMI).
Methods: AMI patients presenting within 12 hours of symptom-onset were randomized to primary stent or PTCA. Baseline serum creatinine was available for 851 patients. Creatinine clearance was calculated using the Cockcroft-Gault formula: Cl=((140-age) x weight)/(72 x serum creatinine); corrected x 0.85 for women. Clinical follow-up was obtained at 6-months.
Results: The mean serum creatinine and creatinine clearance on admission were 1.05 ± 0.35 mg/dL and 89 ± 34 ml/min respectively. Serum creatinine alone did not correlate with in-hospital or six-month event rates. However, by univariate analysis a creatinine clearance of ≤ 75 ml/min (mean creatinine 1.2 ± 0.4 mg/dL) was associated with hypotension in the cath lab (10.6 vs 6.5%, p=0.035), intubation (1.3 vs 0%, p=0.018), in-hospital death (5.1 vs 0.8%, p=0.0001), in-hospital MACE (6.8 vs 3.0%, p=0.01) and death at 6-months (7.4 vs 1.1%, p<0.0001). Creatinine clearance predicted in-hospital and 6-month death in a multivariate model (excluded age and sex since these were used to calculate clearance). Mean contrast volume was not significantly higher for patients with events. Four patients required dialysis post intervention; admission creatinine and creatinine clearance were: 0.7, 1.0, 1.5, 4.1 mg/dL and 80, 95, 53, 22 ml/min in these patients respectively.
Conclusion: Creatinine clearance, but not serum creatinine, on admission is a predictor of early and late death after primary angioplasty or stenting for acute myocardial infarction. These data suggest that routine calculation of admission creatinine clearance may better risk stratify AMI patients.

1249-102 Women With Acute Anterior Myocardial Infarction Have Less Precordial ST Elevation Than Men Independent of Age of Presentation

R. S. Wright, Wayne L. Miller, Ihor Gussak, David L. Dvorak, Thomas P. Aufderheide, John H. Haley, Stephen L. Kopecky, Guy S. Reeder, Stephen C. Hammill. *Mayo Clinic, Rochester, MN*

Introduction: Women who experience acute myocardial infarction (AMI) have significantly higher mortality rates than men. Previous studies have demonstrated that women are treated less aggressively than men. It is not clear why these gender differences exist. It is possible that the electrocardiographic changes in women differ compared to men in AMI. **Populations and Methods:** We analyzed 1366 patients who had digitally stored admission ECG's with acute myocardial infarction (n=1159) and 207 age-matched control patients with non-cardiac chest pain. We subdivided them into age < 60 years (n=402) and age > 60 (n=757) and compared to 207 age matched controls and by whether they were ST elevation or non-ST elevation AMI. We compared the magnitude of ST elevation (STE, expressed in μV) using a new computerized ECG analysis system at the ST-E-point. STE was separated from non STE by the presence of > 50 μV on the index ECG. **Results:** QRS duration was slightly different between women and men in our study population. The QRS duration for females over age 60 was 93+ 16 msec compared to 101+ 22 in males > 60, p=0.001. Such differences were less pronounced in females < 60 (91+ 16 msec) vs males < 60 (96+ 14 msec), p=0.054. We did observe that women had significantly less STE than men independent of age. A computerized ECG program (GE Marquette) using these new findings on admission ECGs improved the sensitivity for detection of anterior acute MI from 42% to 48% for women < 60 years.

ECG Lead	Women <60	Men <60	p-value	Women >60	Men >60	p-value
V2	307±206	432±300	0.007	336±252	421±271	0.009
V3	336±274	478±383	0.017	446±292	528±291	0.023
V4	200±210	323±307	0.010	322±222	419±237	0.0076
V5	107±143	157±155	0.045	190±158	229±183	0.069

Conclusions: It is important to recognize that women have less STE than men with anterior AMI. These differences exist independent of age. It is possible that women with AMI may experience worse in-hospital outcomes and receive less aggressive therapies in part due to these electrocardiographic differences which mask a subset of women with AMI who fail to meet traditional criteria for reperfusion therapy.

POSTER SESSION

1250 Morbidity and Mortality Associated With Surgical Revascularization

Tuesday, March 20, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 4:00 p.m.-5:00 p.m.

1250-79 Factors Associated With the Risk of Stroke Following CABG: Results From the National Cardiovascular Network (NCN)

Elizabeth M. Mahoney, Trevor D. Thompson, Emir Veledar, Joy Burnette, Jeremy Morton, Willis H. Williams, William S. Weintraub. *Emory University School of Medicine, Atlanta, GA*

Background: Stroke is a devastating complication of coronary surgery. Improved ability to identify patients at high risk of peri-operative stroke could be used to improve medical decision making.
Methods: We examined factors associated with risk of peri-operative stroke using a large national outcomes database. Demographic, clinical and peri-operative characteristics were examined in 20,585 patients undergoing CABG at 16 NCN centers between 1/98 and 6/99.
Results: Mean age was 66±11 yrs with 31% female. The incidence of peri-operative stroke was 1.9% (n=398). For patients with stroke, in-hospital mortality was 24.9% as compared to 2.8% for non-stroke patients (p<.0001). Multivariable logistic regression revealed 11 factors independently associated with the risk of stroke, as well as an interaction with sex whereby the risk associated with cerebrovascular disease was greater for men than women. The *c*-index for the model was .74 (.73 from bootstrap validation) indicating very good discrimination

NCN In-Hospital Stroke Following CABG Model

Factor	χ^2 (df)	p-value	Odds Ratio	95% CI
Age (10 yrs.)	41.78 (1)	<.0001	1.47	1.31-1.65
Hx. CVD	53.02 (2)	<.0001		
Female			1.45	1.03-2.05
Male			2.73	2.07-3.61
Bypass Time (20 min)	41.34 (1)	<.0001	1.09	1.06-1.12
Unstable Angina	10.14 (1)	.0015	1.41	1.14-1.75
PVD	8.80 (1)	.0030	1.45	1.13-1.85
Female	10.73 (2)	.0047		
No Hx. CVD			1.50	1.14-1.98
Hx. CVD			0.80	0.55-1.16
Hx. CHF	7.37 (1)	.0066	1.35	1.09-1.68
Hypertension	6.74 (1)	.0094	1.39	1.08-1.78
Renal Insuff.	6.36 (1)	.0117	1.52	1.10-2.10
Diabetes	4.39 (1)	.0362	1.26	1.01-1.56
Wt. (kg.)	9.93 (4)	.0416	non-linear	--

A nomogram can be created from this model which may be useful in identifying patients at high risk of peri-operative stroke.
Conclusion: The risk of peri-operative stroke is increased in older patients, and patients with: previous CVD, prolonged bypass time, unstable angina, peripheral vascular disease, heart failure, hypertension, renal insufficiency, diabetes and/or obesity. Predicted probabilities of peri-operative stroke can be derived from this model in order to identify high-risk patients who may benefit through the consideration of alternative treatment strategies.

1250-80 Hospital Care After Coronary Artery Bypass Grafting Procedures

Elisabeth Stahle, Paul Blomqvist, Johnny Steuer, Anders Ekbom. *Dept Thoracic Cardiovasc Surgery, University hospital, Uppsala, Sweden, Dept Medical Epidemiology, Karolinska institute, Stockholm, Sweden*

Background: After a coronary artery bypass grafting procedure patients still have a substantial risk for readmission to hospital. This risk is partly influenced by an increased morbidity caused by the arteriosclerotic process and related diseases but also the possible need for reinterventions due to progression of the CAD or graftclosure. **Methods:** 7,721 patients underwent primary CABG 1987 through 1996. Follow-up of survival and admission to any swedish hospital was updated in january 1998 by computerized linkage to national registrers. The mean follow-up was 52 months. **Results:** During follow-up 792 patients died corresponding to a survival rate of 95% after one year, 94 % after years and 91 % after 5 years. Early mortality definied as death from any cause before hospital discharge was 3.0 % (229/7,721). 36 % (2,712/7492) of those that survived the first hospital stay needed no hospital readmission. 66 patients out of those died without prior hospitalisation. 4,780 patients were readmitted at 36,073 occasions. First readmission most often occurred within the first postoperative year. Freedom from readmission was 56 % after 1 year and 37 % after 3 years. The absolute vast majority of readmissions were related to some extent to the ischemic heart disease. 2,446 (7 %) admissions were caused by peripheral artery disease, 353 (1 %) by neurological disorders and 276 (1 %) by fractures.Independant riskfactors for readmission among patients surviving surgery was high age (< 60 yrs relative hazard [RH]=1.0, 60-70 yrs RH=1.2, > 70 yrs RH=1.4), hypertension (RH=1.1), diabetic disease (RH=1.3), severely reduced left ventricular func-

tion (RH=1.3) and advanced preoperative NYHA functional class(II-IIIA =1.0, IIIB=1.2, IV=1.3). **Conclusion:** Considering that CABG patients constitute a severely diseased group, the finding that 40 % of the patients did not need readmission within 3 years following surgery, is encouraging and strongly supports complete revascularisation with CABG.

1250-81 Elimination of Cardiopulmonary Bypass Improves Early Clinical Outcome After Coronary Artery Bypass Surgery in Patients With Chronic Renal Insufficiency

Sotiris C. Stamou, Michael Mack, Syma Prince, Albert J. Pfister, Mercedes K. C. Dullum, Paul J. Corso. *Washington Hospital Center, Washington, DC, Medical City Dallas Hospital, Dallas, TX*

Background: Chronic renal insufficiency (CRI) has been associated with a high morbidity and mortality (7-15%) after coronary artery bypass grafting (CABG) with cardiopulmonary bypass (On-pump). It is unknown, however whether CABG without cardiopulmonary bypass (OPCAB) may yield an improved clinical outcome over On-pump CABG in patients with preexisting CRI. **Methods:** We compared the perioperative outcomes of patients with CRI, (baseline serum creatinine > 2.0 mg/dl), who underwent On-pump (n=210) versus OPCAB (n=91), between October 1998 and April 2000. Only patients who received > 1 graft were included. Patients were well matched with respect to the baseline characteristics, except for a higher percentage of male patients (76.4% vs. 60.4%, p=0.008) at the On-pump vs. OPCAB group. **Results:** Early clinical outcome is shown (see table). No patient scheduled for OPCAB required conversion to On-pump CABG. Complete revascularization was achieved in all patients. **Conclusions:** The deleterious effect of CRI on the early clinical outcome after CABG is especially pronounced after On-pump than OPCAB. Pulmonary, cardiac and further renal function deterioration in patients with preexisting CRI may account for this phenomenon and favor OPCAB as a low risk revascularization option at this subset of patients.

	On-pump CABG	OPCAB	p
Prolonged Ventilation	15.7%	5.5%	0.014
Low Cardiac Output	13.8%	1.1%	<0.001
Hemodialysis	9.5%	2.5%	0.028
Packed red blood cell units	4.7 (SD=3)	3.1 (SD=2)	0.046
Operative mortality	10.0%	4.4%	0.12

1250-82 Early Mortality And Morbidity of Bilateral Versus Single Internal Thoracic Artery Revascularization: Propensity and Risk Modeling

Demosthenes Katritsis, John Ioannidis, Othon Galanos, Cliff P. Connery, George Drossos, Daniel G. Swistel, Constantine Anagnostopoulos. *ATHENS EUROCLINIC, ATHENS, Greece*

Objective. We examined whether bilateral internal thoracic artery (BITA) revascularization is associated with any increased in-hospital mortality and complications compared with single internal thoracic artery (SITA) revascularization. **Background.** Despite proven long-term benefits, BITA revascularization has been slow to adopt because of fear of increased early morbidity. **Methods.** We evaluated 1697 consecutive patients undergoing BITA (n=867) or SITA (n=830) revascularization. We used propensity score analyses and adjusted risk models to address differences between arms. **Results.** There were 20 (2.3%) deaths in the BITA group vs. 26 (3.1%) in the SITA group (odds ratio 0.73, p=0.30). Propensity analysis identified several parameters that affected the decision to use BITA. Adjusting for propensity score and all potential risk factors, the odds ratio for death with BITA vs. SITA was exactly 1.00. BITA did not increase the number of in-hospital complications with the possible exception of deep sternal wound infections (11 [1.3%] vs. 3 [0.4%], p=0.057). In multivariate modeling BITA increased the risk of deep sternal wound infections only in emergent cases and in older patients; the excess risk was negligible among 1206 patients (71.1% of total) who did not have emergent revascularization and were *70 years old (risk difference 0.3%, p=0.74). There was no difference in length of stay after adjustment for propensity factors (mean 11.3 vs. 11.7 days, p=0.66). **Conclusions.** BITA grafting confers no increased risk for early death and does not prolong hospital stay. The small increase in the risk of deep sternal wound infections does not affect the majority of patients.

1250-83 Clopidogrel for Prevention of Thrombotic Complications After Cardiac Surgery: A Word of Caution

Mercedes K. C. Dullum, Borjanka O. Leiboff, Sotiris C. Stamou, Peter C. Hill, Steven W. Boyce, Albert J. Pfister, Ammar S. Bafi, Robert C. Lowery, Qazi Anjum, Jorge M. Garcia, Paul J. Corso. *Washington Hospital Center, Washington, DC*

Background: Clopidogrel is a relatively new platelet aggregation inhibitor, but both its efficacy and its safety as a pharmacological adjunct to cardiac surgery have not been fully elucidated.

Methods: We retrospectively analyzed the patients who underwent coronary artery bypass surgery (CABG, n=979), valve replacement (n=95) or CABG plus valve replacement (n=126) between January and August 2000. We compared the early clinical outcome between two groups: Group A who received preoperative clopidogrel (75 mg, once per day, orally) and aspirin (325 mg, once per day), (n=121) and Group B who received aspirin alone (325 mg, once per day), (n=1079). Early thromboembolic and hemorrhagic complications were recorded in patients from both groups. Patients from the two groups were comparable with respect to baseline characteristics.

Results: Comparative analysis is summarized in Table.

Complications	Group A (n=121)	Group B (n=1079)	p
Hemorrhagic			
Postoperative transfusions	61%	45%	0.001
Reoperation for bleeding	3%	2%	0.32
Gastrointestinal bleeding	7%	1%	<0.001
Thromboembolic			
Pulmonary embolism	2%	1%	0.38
Deep venous thrombosis	0%	0.2%	1
Stroke	2%	3%	0.57
Acute myocardial infarction	1%	0.4%	0.41

Conclusions: Clopidogrel plus aspirin preoperative has a significantly higher rate of postoperative hemorrhagic complications than aspirin alone.

POSTER SESSION

1251 Myocardial Infarction and Ischemia: Focus on Nitric Oxide and Coronary Flow

Tuesday, March 20, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 4:00 p.m.-5:00 p.m.

1251-84 Basal Nitric Oxide Synthesis in Coronary Stenoses: Relation to Morphology, Length, Severity

Dimitris Tousoulis, Costas Tentolouris, George S. Goumas, Costas Xenakis, Tom Crake, Costas Toutouzas, Aris Androulakis, Christodoulos Stefanadis, Graham Davies, Pavlos Toutouzas. *Hippokration Hospital, Athens, Greece, Hammersmith Hospital, London, United Kingdom*

Background: Nitric oxide(NO), a major component of endothelium derived relaxing factor, is synthesized from the amino acid L-arginine by a family of enzymes.The synthesis of NO is competitively inhibited by NG-monomethyl-L-arginine (LNMMA). The effect of inhibition of NO synthesis on coronary stenoses in relation to their geometric characteristics is unknown. **Methods:** In 28 patients(24 male, 4 female) with coronary artery disease (CAD) and chronic stable angina, normal saline (NS) and 4 ìmol/min LNMMA were infused intracoronary, each for 4 minutes, followed by an intracoronary bolus of 250 ìg nitroglycerin(GÓÍ). Coronary stenoses were classified as smooth (smooth concentric or eccentric with regular borders) or irregular. The diameter of 26 smooth and 12 irregular coronary stenoses and their adjacent reference (R) segment was measured by computerized quantitative angiography. **Results:** The mean (+SEM)% change from baseline was:

	NS	LNMMA	GTN
Smooth stenoses	0.3±0.5	-1.8±0.8	11.2±2.1
R segments	1.0±0.3	-1.7±0.8	8.3±1.5
Irregular stenoses	1.0±0.7	-7.0±1.6*+	19.3±3.6*+
R segments	0.9±0.4	-1.2±1.1	10.8±2.1

*=p<0.01 vs smooth stenoses, +=p<0.01 vs R segments.

The severity of stenoses at baseline correlated with the magnitude of LNMMA response irrespective of the type of morphology (p<0.01), whereas there was a weak correlation (r=0.39, p<0.05) between length of stenoses and the magnitudeof constriction to LNMMA. No correlation was found between eccentricity ratio and the response to LNMMA (p=NS). **Conclusion:** In patients with CAD, irregular coronary stenoses constrict significantly more than smooth stenoses, following inhibition of nitric oxide synthesis with LNMMA. This enhanced constriction is focal at the site of stenoses than at the adjacent reference segment. The degree of response to LNMMA is related to stenoses length and stenoses severity and is unrelated to eccentricity ratio.

1251-85 Amelioration of Ischemia- and Reperfusion-Induced Myocardial Injury by Raloxifene: Roles of Nitric Oxide and the Opening of Calcium-Activated Potassium Channels

Hisakazu Ogita, Masafumi Kitakaze, Koichi Node, Hiroshi Asanuma, Shoji Sanada, Seiji Takashima, Masanori Asakura, Yulin Liao, Yoshiro Shinozaki, Hidezo Mori, Tsunehiko Kuzuya, Masatsugu Hori. *Osaka University Graduate School of Medicine, Suita, Japan*

Background: 17β-Estradiol reduces myocardial infarct size via nitric oxide (NO) and the opening of calcium-activated potassium (K_{Ca}) channels. Raloxifene, a selective agonist of estrogen receptors, is reported to cause acute coronary artery vasorelaxing effects. We investigated whether raloxifene reduces infarct size, and what mechanisms are involved in the effects.**Methods:** In the anesthetized open chest beagle dogs, the left anterior descending coronary artery (LAD) was canulated and perfused with blood from the left carotid artery through an extracorporeal bypass tube. We occluded the LAD for 90 minutes followed by 6 hours of reperfusion. Infarct size was measured by TTC staining. Infusion of raloxifene (5μg/kg/minute) into the LAD through an extracorporeal bypass tube was initiated 10 minutes before coronary occlusion and continued up to 1 hour of reperfusion except the coronary occlusion period.**Results:** Heart rate (134 +/- 4 beats/minute) and mean arterial blood pressure (100 +/- 3 mmHg) remained stable throughout the study and were not significantly different among groups. Infarct size was significantly

reduced in the raloxifene group compared with the control group (6.8 +/- 4.2% vs 40.9 +/- 3.9% of the area at risk, p<0.01). Both N^G-nitro-L-arginine methyl ester (an inhibitor of NO synthase) (infarct size: 22.8 +/- 5.4%, p<0.05 vs either raloxifene or control group) and charybdotoxin (a blocker of K_{Ca} channels) (infarct size: 23.5 +/- 5.1%, p<0.05 vs either raloxifene or control group) attenuated the infarct size-limiting effect of raloxifene.**Conclusion:** Raloxifene reduces myocardial infarct size by NO and the opening of K_{Ca} channel-dependent mechanisms in canine hearts.

1251-86 Endothelial Constitutional Nitric Oxide Synthase Gene Polymorphism Is Associated With Coronary Vasospasm

Yuan He, Masahiro Yasutake, Yoshifumi Tomita, Yoshiki Kusama, Morimasa Takayama, Kazuo Munakata, Teruo Takano. *Nippon Medical School, Tokyo, Japan*

Background: Nitric oxide (NO) exerts various pathophysiological effects on the cardiovascular system and there was a reduction of NO activities in both coronary and brachial arteries of the patients with coronary vasospasm. Recently, it has been reported that endothelial constitutional nitric oxide synthase (ecNOS) gene intron 4 polymorphism is one of the genetic factors to control plasma NO. However, the correlation between ecNOS gene polymorphism and coronary vasospasm has not been thoroughly investigated. **Methods:** In this study, 60 admitted patients with chest pain were investigated. Coronary vasospasm was provoked by the intracoronary administration of acetylcholine in all patients and the lumen diameters of large epicardial coronary arteries were assessed by quantitative coronary arteriography. According to the presence or absence of coronary vasospasm, the patients were divided into two groups, coronary vasospasm group (CVS; n=42, male/female=2.0, 57.3±10.8 years) and control group (control; n=18, male/female=0.8, 58.4±10.8 years). The intron 4 polymorphism of ecNOS gene was then determined by polymerase chain reaction method. **Results:** The incidence of a/b genotype of ecNOS gene was significantly higher in CVS than that in control (0.40:0.11, p=0.025) with no presence of a/a genotype. The ratio of smokers was higher in CVS than that in control (0.60:0.28, p=0.02) and other conventional coronary risk factors such as hypertension, diabetes mellitus, hyperlipidemia, BMI and serum level of lipids showed no significant differences between two groups. Furthermore, there were 17 cases with a/b genotype and 25 cases with b/b genotype in CVS. The incidence of multi-vessel spasm and diffuse spasm was significantly higher in a/b genotype than in b/b genotype (0.88:0.52, p=0.0145; 0.76:0.48, p=0.065). Stepwise multivariate regression analysis on gene polymorphism and the conventional coronary risk factors showed that smoking and a/b genotype were the independent factors to predict coronary vasospasm (F=5.364 and 5.297 respectively; p=0.02). **Conclusion:** It suggested that ecNOS gene a/b genotype as well as smoking habit might be the key factors to coronary vasospasm.

1251-87 The Dihydropyridine Ca Channel Blocker, Nifedipine, Limits Infarct Size via Bradykinin- and NO-Dependent Mechanisms in Dogs

Masafumi Kitakaze, Yoshiro Shinozaki, Hidezo Mori, Hiroshi Asanuma, Shoji Sanada, Masanori Asakura, Hisakazu Ogita, Yulin Liao, Koichi Node, Seiji Takashima, Tsunehiko Kuzuya, Masatsugu Hori. *Osaka University Graduate School of Medicine, Osaka, Japan*

Recently, dihydropyridine Ca channel blockers, such as amlodipine, are reported to increase NO levels of coronary vessels. We have also reported that either nifedipine or benidipine increases the cardiac NO levels and coronary blood flow in the ischemic hearts. Since NO is cardioprotective, affecting the coronary circulation, myocardial metabolism, and neurohumoral factors such as the renin-angiotensin system and the sympathetic nerve system, nifedipine may limit infarct size via NO-dependent mechanisms. To test this idea, 49 beagle dogs were studied. In the open chest dogs, the left anterior descending coronary artery was perfused with blood through a bypass tube and occluded for 90 min followed by 6 hours of reperfusion. Infarct size was assessed by TTC staining. When nifedipine of 3 or 6 ug/kg/min was infused into the bypass tube between 10 min prior to the onset of ischemia and 60 min of reperfusion, systemic blood pressure did not change significantly during infusion of nifedipine (102 +3 or 96+4 mmHg at the onset of ischemia and 60 min of reperfusion, respectively). Infarct size was reduced by the administration of nifedipine (3 or 6 ug/kg/min) compared with the untreated condition (25.6+2.6 and 19.1+3.5 vs. 43.4+5.6%, respectively), which was completely blunted by L-NAME (45.0+3.6 and 45.4+4.2 vs. 47.9+3.9% in the nifedipine (3 or 6 ug/kg/min) with L-NAME (10 ug/kg/min) groups vs. the L-NAME group). Furthermore, the antagonist of bradykinin B2 (HOE140) also blunted the infarct size limitation of nifedipine (39.8+3.1 vs. 43.2+2.9% in the nifedipine (6 ug/kg/min) with HOE140 (10 ng/kg/min) groups vs. the HOE140 group). There were no significant differences in collateral blood flow assessed by the microsphere method at 45 min of ischemia between each group (7.8+1.8 ml/100g/min). We conclude that nifedipine limits infarct size via bradykinin- and NO-dependent mechanisms. The cardioprotective effect of nifedipine against ischemia and reperfusion injury may be partially attributed to NO.

1251-88 Ischemia-Selective Early Increase in Nitric Oxide Synthesis Confer Acute Cardioprotection Against Myocardial Infarction Afforded by Pravastatin

Shoji Sanada, Masafumi Kitakaze, Hiroshi Asanuma, Seiji Takashima, Koicki Node, Hisakazu Ogita, Masanori Asakura, Yulin Liao, Tsunehiko Kuzuya, Masatsugu Hori. *Osaka university Graduate School of Medicine, Suita, Japan*

Background; HMG-CoA reductase inhibitors (statins) reduce the risk for cardiovascular diseases independent of cholesterol-lowering effect. Although nitric oxide (NO) is thought to mediate this mechanism, no study has clarified the acute cardioprotection and NO synthesis by statins. We tested whether pravastatin acutely limit infarct size, and whether NO and neutrophil infiltration are involved. **Methods;** In open-chest beagle dogs, coronary artery was occluded for 90 minutes followed by 6-hours of reperfusion. In other dogs, the continuous low flow studies were performed. **Results;** Collateral flow and percent risk area were consistent for all groups. Pravastatin (2mg/kg) reduced myeloperoxidase activity in the border region of the ischemic myocardium (Mean+SEM.: 7.6+2.8 vs. 22.8+6.0unit control, p<0.01) and infarct size (22.6+4.5 vs. 37.1+4.2% control, p<0.05), which was blunted by preischemic and postischemic NO synthase inhibition by Nw-nitro-L-arginine methyl ester (L-NAME) (22.1+4.6unit and 36.8+4.1%), not by only preischemic L-NAME treatment (11.9+4.2unit and 26.1+5.3%). In the continuous hypoperfusion studies with low coronary blood flow (CBF) or low coronary perfusion pressure (CPP), pravastatin increased the differences in the level of NO metabolites between coronary venous and arterial blood (15.6+2.3 vs. 9.3+1.5nmol/L control under constant CBF, p<0.05) and coronary blood flow (57+3.2 vs. 44+2.6mL/100g/min control under constant CPP, p<0.05) only under hypoperfusion after 3 hours, whereas not under normoperfusion (6.0+1.2 vs. 5.3+1.3nmol/L control, and 99+4.6 vs. 96+5.0mL/100g/min control). **Conclusion;** Pretreatment with pravastatin confers the ischemia-selective early increase in NO production and NO-dependent acute infarct size-limitation, which might be associated with the inhibition of regional neutrophil infiltration in vivo.

1251-89 Regional Myocardial Function in Chronic Total Coronary Occlusions and Its Relation to the Collateral and Peripheral Myocardial Resistance

Gerald S. Werner, Oliver Gastmann, Barbara M. Richartz, Markus Ferrari, Hans R. Figulla. *Clinic Internal Medicine III; Friedrich-Schiller-University, Jena, Germany*

Background: Collateral function in chronic total coronary occlusions (TCO) is determined by the resistance of the collaterals (Rc) and the myocardial resistance distal to the occlusion (Rp). The aim of this study was to study the relation between the collateral function and the functional integrity of the myocard distal to the occlusion.
Patients: We studied 26 patients with a TCO of at least 4 weeks duration before the occlusion was reopened by PTCA, and after the recanalization procedure was completed with stenting. We measured aortic pressure (Pao), intracoronary pressure distal to the occlusion (Po) by a pressure wire, and the intracoronary flow velocity integral distal to the occlusion before (Vo) and after recanalization (Va) by a Doppler wire. The resistance was calculated as Rp=Po/Vi, and Rc as (Pao-Po)/Vi. The measurement of Vo and Po were done before the first balloon inflation, and 45 min later after PTCA with a repeat balloon occlusion. 14 Patients with a well preserved regional function (group N) were compared with 12 patients with a severely impaired regional function (group I).
Results: Rc, Rp and Vo are summarized for both groups before and after recanalization in the (table; differences between groups: * p=0.08; † p<0.05; changes before and after PTCA within each group for all 3 parameters: p<0.001).

	group N		group I	
	Before PTCA	After PTCA	Before PTCA	After PTCA
Vo (cm)	11.9±5.6	5.8±2.6	10.8±11.0	5.7±6.4
Rc (mmHg/cm)	6.6±4.4	14.7±9.5	10.2±6.7*)	28.5±24.3†)
Rp (mmHg/cm)	4.9±3.3	7.5±4.4	6.8±4.4	13.7±11.6†)

Rc tended to be lower in group N before PTCA, Vo and Rp were similar. After PTCA Rp and Rc increased in both groups significantly, while Vo dropped by more than 50%. The increase of Rc and of Rp was smaller in group N than in group I. Well preserved regional function distal to an occlusion lead to a lower Rc and to a lower Rp after PTCA.
Conclusion: Specific differences in collateral function were found in TCO which were related to the preserved regional ventricular function distal to the occlusion. Collateral function changed instantaneously by the reopening of a TCO. Lower Rp and Rc after PTCA with normal regional function could indicate a higher degree of remaining collateral function.

1251-90 Why Does Severe Coronary Stenosis Decrease Perfusion Reserve in the Remote Myocardium?

Olaf M. Muehling, Prasad Panse, Andrey Zenovich, Fan Zhao, Yimei Huang, Abdul Mansoor, Michael Jerosch-Herold, Norbert M. Wilke. *Center for Cardiovascular MRI of the Department of Radiology at the University of Minnesota, Minneapolis, MN, Division of Cardiology of the Department of Medicine at the University of Minnesota, Minneapolis, MN*

Background: We determined myocardial blood flow (MBF) and vascular resistance with quantitative MR first-pass (MRFP) imaging to assess the underlying mechanism of a reduced perfusion reserve (PR, hyperemia/rest perfusion) in remote myocardium due to severe single-vessel disease.
Methods: MRFP-imaging was performed in 24 pigs with a 1.5T MRI (Siemens). One week before imaging a severe stenosis (>90%) was induced by placing a hollow bead in the left circumflex artery (LCx) in 12 pigs (Group A). Group B had normal coronary arteries. Signal intensity curves were generated from the images with ARGUS software (Siemens). Blood flow estimates (MBF, ml/g/min) were determined from the curves with former validated Fermi-model constrained deconvolution. Myocardial vascular resistance (MVR) was calculated as mean blood pressure (BP)/MBF (mmHg*g*min/ml). MBF and MVR were determined at rest and hyperemia (by a maximal vasodialating dose of adenosine) in stenosis-dependent and remote (antero-septal) myocardium of A and the corresponding LCx- and left anterior descending (LAD)-region of B. MBF was normalized for the rate pressure product (RPP) (MBF x mean group/individual RPP).

Results: MBF at rest in remote myocardium of A was elevated vs. B as a result of a decreased MVR. Hyperemic MBF in the remote myocardium of A was decreased vs. B along with a decreased BP.

	Rest		Hyperemia	
Group	A (LCx-stenosis, LAD remote)	B	A (LCx-stenosis, LAD remote)	B
MBF LC	0.9±0.2	1.1±0.2†	1.2±0.3	3.1±1.2†
LAD	1.5±0.3*	1.2±0.3†	2.0±0.8*	3.4±1.3†
MVR LC	121±71	122±25	70±24	45±16†
LAD	62±18*	123±41†	44±9*	43±21
BP (mmHg)	85±6	133±7†	78±11	124±16†
HR (1/min)	102±25	114±13	136±34	138±27
PRP (mmHg/ms)	0.14±0.03	0.25±0.03†	0.18±0.05	0.29±0.09†

* p<0.02 vs. stenosis, † p<0.04 vs. A, § p<0.05 vs. Rest

PR was reduced in A vs. B in stenosis-dependent (1.5± .3 vs. 2.4± .7, p< .01) and remote myocardium (1.3± .3 vs. 2.9± .9, p< .01) with no significant difference between the regions in A.

Conclusion: A reduced resting MVR of possible metabolic origin and a reduced coronary perfusion pressure at hyperemia cause an increase in rest and a reduction in hyperemic MBF resulting in a decreased PR of the remote myocardium in severe single vessel disease.

POSTER SESSION

1252 Stabile Ischemic Syndrome: Pathophysiology, Diagnosis, and Prognosis II

Tuesday, March 20, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 4:00 p.m.-5:00 p.m.

1252-91 Silent Ischemia During Daily Life Is Related to Increased Thrombin Generation in Patients With Chronic Stable Angina

Ignatios Ikonomidis, Felicitta Andreotti, Christodoulos Stefanadis, Christos Pitsavos, Emanuel Economou, Pavlos Toutouzas, Petros Nihoyannopoulos. *Hammersmith Hospital, London, Greece, Ippokration Hospital, Athens, Greece*

Background: Patients with chronic stable angina (SA) and silent ischemia during daily life usually present complex and thus potentially thrombogenic atheromatous plaques at coronary angiography. We investigated whether thrombin generation, platelet activation or high plasma levels of procoagulant cytokines are related to silent ischaemia in SA and whether reduction of the above factors by aspirin (ASA) is associated with reduction of silent ischaemia. **Methods.** We measured prothrombin fragments (PF1+2, nmole/l),macrophage colony stimulating factor (MCSF), inerleukins 1b (IL1b) and 6 (IL6) (pg/ml) plasma levels and 24h urine excretion of 11 dehydrothromboxane B2 (DTXB2, ng/mg creatinine) in 60 patients with SA and in 24 matched controls. Samples and urine collections were obtained at the end of a 48h Holter (HM). Patients had angiographically documented disease. Fourty had ischaemia at HM and were randomly treated with ASA 300mg, o.d. or placebo for 3 weeks in a double blind, cross-over trial. **Results.** PF1+2, MCSF, and IL6 were increased in patients compared to controls (p<0.05). Patients with ischaemia at HM had higher MCSF and DTXB2 compared to those without (MCSF: 1124±651 vs 528±417, DTXB2: 4.2±3.2 vs 2.3±1.9, p<0.01). Only patients with silent ischaemia (20/60) had higher PF1+2 than patients with both silent and symptomatic episodes (20/60) or patients with no ischemia (20/60) (PF1+2: 2.26±1.8 vs 1.73±1.2 vs 0.93±0.5, p<0.01). MCSF was related to DTXB2 before and after ASA treatment (r=0.47 and r=0.50, p<0.01). ASA reduced cytokine levels, PF1+2, DTXB2 (p<0.05) as well as the number and duration of silent ischemic episodes (number before ASA: 6.5±1.1 vs 3±1.0 after ASA, p<0.01 and duration (min) before ASA: 26±5 vs 15±4.2 after ASA, p<0.01) with no effect on symptomatic episodes. **Conclusion.** Daily life ischemia in patients with SA is related to increased platelet activation induced by high cytokine levels. Only silent ischemia is related to increased thrombin generation and is reduced by aspirin possibly due to the anticoagulant and antiinflammatory effect of the drug.

1252-92 Circadian Variations of Silent and Symptomatic Ischaemia in Patients With Stable Coronary Insufficiency

François Allaert, Marianne Zeller, Christian Caussé, Gabriel Laurent, Jean-Pierre Marcantoni, Jean-Eric Wolf. *CHU, Dijon, France*

Background: The aim of the study was 1) to determine in standard living conditions the circadian variations of the symptomatic and silent electrocardiographic ischaemia in patients with chronic stable coronary insufficiency and 2) To evaluate the influence of the past history of the patients on the circadian variations of the symptomatic and silent ischaemic events. **Methods:** The patients included in the study presented, with stable angina pectoris and have undergone a 96 hours Ambulatory ECG (AECG) monitoring with a low-weight and compact material which did not modify their daily activities (Rtest). The system records the trace that the patient has initiated by himself following the onset of symptoms and makes possible to distinguish between silent and symptomatic ischaemia. The same experienced cardiologist validated all the AECG records. **Results:** 1022 patients aged 64.6 +/- 11.0 years have undergone an electrocardiographic record by an R-test. During the recordings, 751 patients (73.5%) did not present any ECG sign of myocardial ischaemia, 148 (14.5%) presented only silent ischaemia, 92 (9.0%) silent ischaemia and symptomatic ischaemia, 31 (3.0%) of symptomatic ischaemia only. These results show that more than one patient in two (54.66%) (148/271) presenting myocardial ischaemia is clinically asymptomatic. Of the 3258 recorded ischaemic events, only 9% (n=295) were symptomatic. Important circadian variations of ischaemia are noticed. The frequency of these events increases suddenly from 7 AM culminating at 10 AM and then decreases quickly until after till 2 PM. The pattern then increases again from 2 PM to 5 PM and decreases gradually during the evening to reach to a threshold of low incidence until the early morning. **Conclusion:** The circadian variations of silent myocardial ischaemia and in particular the increase in the frequency if ischaemic events early in the morning chronologically correspond with the variations of the symptomatic ischaemia observed in the study. They are also related with the sudden rise of the blood pressure and the peak of frequency of myocardial infarction described in the literature during this period.

1252-93 Ultra Long-Term Prognosis of Vasospastic Angina With Normal Coronary Arteriogram Treated by Calcium Channel Antagonists: Results From Twenty-Year Prospective Follow-Up Study

Kenichi Ito, Masakazu Yamagishi, Hiroshi Tsutsui, Kazuo Haze, Tetsuya Sumiyoshi, Kenichi Fukami. *National Cardiovascular Center, Suita, Japan*

Background: Although the patients (pts) with vasospastic angina treated with calcium channel antagonists have relatively good outcome, few data exist regarding ultra long term prognosis particularly in pts with normal coronary angiography. Therefore, we studied the relationship between the ultra long term outcome of vasospastic angina prospectively followed up to 20 years and the factors influencing the prognosis. **Methods:** Total 193 pts (163 men and 30 women with mean age of 54 ± 8.0) who had angiographic evidence of intense coronary vasospasm without preexisting disease at the sites of vasospasm were enrolled and prospectively followed to 20 (mean 12± 5.2) years. Cardiac events consisted of the cardiac death and the ischemic events which included acute myocardial infarction and unstable angina. Cox analysis, that was used to identify potentially important prognostic variables, selected coronary risk factors such as hypertension, diabetic mellitus, hyperlipidemia and history of smoking. **Results:** Cardiac death occurred in 10 pts (5.2%) and the ischemic events in 31 pts (16%) during the follow up period. Under these conditions, hyperlipidemia (OR=0.28, 95% CI=0.087-0.14, P=0.035) was the only independent predictor of event-free survival by the Cox analysis. Kaplan-Meier survival analysis revealed a event-free survival curve in vasospastic angina with normal coronary (survival rate; 5yrs, 10yrs, 15yrs, and 20 yrs, 85.5%, 79.6%, 76.5%, and 73.9 % respectively). **Conclusions:** These results demonstrate that vasospastic angina with normal coronary angiography treated with calcium channel antagonists has good outcome. Under these conditions, the most important factor affecting the prognosis is revealed to be hyperlipidemia that might alter underlying coronary endothelial function. We suggest that intensive management of hyperlipidemia should be considered even with normal coronary angiography.

1252-94 Minimal Coronary Artery Disease Is Associated With Persistent Chest Pain in Women: Results From the NHLBI-Sponsored WISE Study Coronary Angiographic Core Laboratory

Barry L. Sharaf, B. Delia Johnson, Marian B. Olson, Carl J. Pepine, Steven E. Reis, William J. Rogers, Nathaniel Reichek, C. Noel Bairey Merz. *Rhode Island Hospital and Brown University School of Medicine, Providence, RI*

Background: Many women presenting with chest pain suspected to be ischemic, have persistent symptoms at follow-up despite coronary angiography identifying no significant stenosis (<50%). **Methods:** In order to identify angiographic predictors of persistent chest pain at 1 year follow up, we performed a detailed quantitative angiographic analysis (QCA) of coronary angiograms from 142 women with (43%) and 186 without (57%) persistent chest pain all of whom initially presented with symptoms believed to be ischemia and were enrolled in the Women's Ischemia Syndrome Evaluation (WISE) study but who were found to have no > 50% stenosis at coronary angiography. **Results:** Women with persistent chest pain were younger (54±10 vs 58±11 years, p=0.001 respectively) than those without. Overall angiographic severity score was higher in those women with chest pain (7.4±4.1 vs 7.1±3.9 respectively, p=0.06 controlling for age) than in those without. Importantly, 46% of the women with versus only 41% of those without (p=0.05 controlling for age) had minimal (as opposed to none) coronary artery disease (20-49% stenoses). Overall ejection fraction, coronary artery size and evidence for complex plaque was not different between the 2 groups. There was a trend towards slower flow in women with persistent chest pain versus without, with TIMI Frame Count >40 in 14% vs 7% (p=.17) respectively. There was also a trend towards worse endothelial function in those women with versus without symptoms at follow-up with 62% versus 41% (Left Main), 61% versus 53% (LAD) and 52% versus 37% (LCX) having an abnormal vasomotor response to intra-coronary Acetylcholine (all p=ns) respectively. **Conclusion:** We conclude that the coronary angiographic findings in women without significant CAD but with persistent chest pain are different than in those women who become asymptomatic. Women with symptoms more often have evidence of early CAD as measured by QCA, flow and endothelial function. These are women who should be targeted for aggressive risk factor modification.

POSTER SESSION

1253 Evolving Antithrombotic Approaches in Acute Coronary Syndromes

Tuesday, March 20, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 4:00 p.m.-5:00 p.m.

1253-95 Enoxaparin Versus Tinzaparin in the Management of Unstable Coronary Artery Disease (EVET Study)

Lambros K. Michalis, Nicolaos Papamichail, Christos S. Katsouras, Ageliki Karahaliou, Eleni Sourla, John Novas, Lambros Sioros, Andreas Papalambrakopoulos, John A. Goudevenos, Dimitris A. Sideris. *University Hospital of Ioannina, Ioannina, Greece*

Low molecular weight heparins are rapidly emerging as an alternative form of antithrombotic therapy to the standard unfractionated heparin. These drugs inspite of similarities in origin, synthesis and structure, have different pharmacokinetic and pharmacodynamic characteristics and possibly elicit different efficacy. The aim of the present study was to compare head to head the efficacy of enoxaparin versus tinzaparin in the management of acute coronary syndromes. Methods. In a prospective study 438 patients with unstable angina or non Q-wave myocardial infarction were randomized to receive either subcutaneous injections of 100 UI/kg enoxaparin twice daily (N=220) or 175 UI/Kg tinzaparin once daily (N=218) for 7 days. The primary end-points were death, myocardial infarction, refractory angina and recurrence of unstable angina. Secondary end points were rehospitalisation due to unstable angina or myocardial infarction, death and need for revascularisation at 30 days. Results. At 7 days recurrence of unstable angina occurred less frequently in the enoxaparin than in the tinzaparin group (24/220 vs 41/218, p=0.029). No statistical significant differences were observed between these 2 groups with respect to death, myocardial infarction or refractory angina at 7 days. At 30 days there were no differences between the 2 groups regarding rehospitalisation and death. The need for revascularisation at 30 days was significantly less frequent in the patients assigned to enoxaparin (36/220 vs 57/218, p=0.019). Bleeding complication rates were similar in the two groups. Conclusions. Antithrombotic treatment with enoxaparin for 7 days was more effective than tinzaparin in reducing the incidence of recurrent angina in patients with unstable angina or non-Q wave myocardial infarction in the early phase. Enoxaparin recipients had also significantly reduced need for revascularisation at 30 days. This benefit was achieved without an increase of bleeding complications.

1253-96 Safety and Efficacy of Unfractionated Heparin (UH) Versus Enoxaparin (E) in Obese Patients and Patients With Renal Impairment: Analysis From ESSENCE and TIMI 11B Studies

Stephanie M. Inverso, Marc Cohen, Elliott M. Antman, Sarah A. Spinler, for the ESSENCE and TIMI 11B Investigators. *Philadelphia College of Pharmacy at the University of the Sciences in Philadelphia, Philadelphia, PA*

Background: There is no published data evaluating low-molecular-weight heparins in obese and renally-impaired patients with acute coronary syndromes.
Methods: The composite endpoint of death, myocardial infarction or urgent revascularization (D/MI/UR) at 43 days, as well as major bleeding and any bleeding (measured during the weight-adjusted treatment phase of the initial hospitalization) were compared between subgroups of patients: obese (N=3439) versus non-obese (N=3558) and renal impairment (N=143) versus no renal impairment (N=3558) from ESSENCE and TIMI 11B.
Results: In obese and non-obese patients, E significantly decreased the risk of D/MI/UR when compared to UH (RR 0.88, p=0.0006 and RR 0.90, p=0.002). Similar major bleeding rates were observed between UH and E in obese patients (0.9% vs 0.7%) and non-obese patients (1.2% vs 1.8%). There was less major bleeding in the obese treated with E compared to the non-obese (RR 0.55, p=0.003). E significantly decreased the rate of D/MI/UR in patients without renal impairment (RR 0.91, p=0.003). An increased risk of D/MI/UR was seen in patients with renal impairment receiving UH when compared to those with no renal impairment (RR 2.1, p=0.004). There was no difference in the rate of D/MI/UR in those with and without renal impairment receiving E (18.8% vs 15.7%). Increased rates of major bleeding were observed in patients with impaired renal function compared to those with no renal impairment receiving both E (7.5% vs 1.2%, p=0.002) and UH (5.8% vs 1.0%, p=0.001). Similarly, there was an increase in any bleeding in patients with renal impairment compared to those with no renal impairment receiving both E (17.9% vs 9.8%, p=0.028) and UH (18.8% vs 3.9%, p=0.001).
Conclusion: E significantly reduced the risk of D/MI/UR at 43 days in obese, non-obese and patients without renal impairment. A reduction in D/MI/UR was not discerned with E in patients with renal impairment perhaps due to small sample size. Similar to other trials, obesity did not increase the risk of D/MI/UR and less major bleeding occurred in obese patients. Renal impairment is a risk factor for bleeding with both UH and E. Large clinical trials focusing on patients with renal impairment are needed.

1253-97 The Use of Enoxaparin and IIb/IIIa Antagonists in Acute Coronary Syndromes, Including PCI: Final Results of the NICE 3 Study

James J. Ferguson, Elliott M. Antman, Eric R. Bates, Marc Cohen, Nathan R. Every, Robert A. Harrington, Carl J. Pepine, Pierre Theroux, The NICE 3 Investigators. *Texas Heart Institute, Houston, TX*

Background: Although recent clinical trials such as ESSENCE and TIMI 11B have shown enoxaparin to be clinically superior to UF heparin for the treatment of ACS, the use of LMW heparins in this clinical situation has been significantly limited by concerns about the safety of combining them with IIb/IIIa antagonists, and logistical issues about making the transition to the cath lab in patients who have already received subcutaneous LMW heparin.
Methods and Results: NICE 3 was a multicenter (46 sites;US and Canada), non-randomized, open-label, observational study to assess the safety profile of enoxaparin, 1 mg/kg sc bid, plus a IIb/IIIa antagonist (tirofiban, n=217; eptifibatide, n=252; or abcximab, n=147) in ACS patients. Patients were initially treated with enoxaparin and a IIb/IIIa antagonist; the choice of IIb/IIIa antagonist was assigned by institution. If PCI was required, combination therapy was continued through the time of the procedure; if the last enoxaparin dose was > 8 hours prior to PCI, an additional iv bolus of 0.3 mg/kg was used at the time of the procedure. The primary endpoint of the study was the incidence of non-CABG major bleeding (n-CABG MB) during the hospitalization, compared to a rate of 2% estimated from prior studies. Secondary endpoints included clinical outcomes.

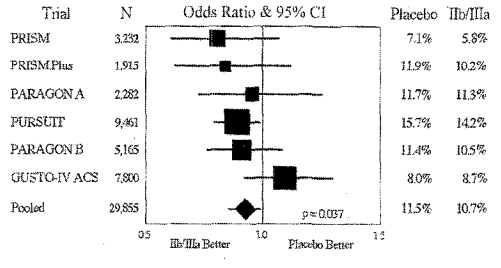
	Tirofiban	Eptifibatide	Abciximab	All IIb/IIIa
All Patients (n = 616)				
Non-CABG major bleeding	1.4 %	3.2 %	0.7 %	1.9 %*
Death	0.5 %	0.4 %	0	0.3 %
MI	4.1 %	3.2 %	2.7 %	3.4 %
Urgent TVR	3.2 %	2.7 %	0.7 %	2.1 %
Platelets < 100K	1.4 %	0.8 %	0	0.9 %
30% Decrease in platelets	3.8 %	4.7 %	9.4 %	5.5 %
PCI Patients (n = 292)				
Non-CABG major bleeding	0.9 %	2:4 %	0	1.0 %

* - p=NS compared to historical estimate of 2 %
Conclusions: 1) The combination of enoxaparin and a IIb/IIIa antagonist does not result in an excess of non-CABG major bleeding; 2) patients on combination therapy can safely undergo PCI; 3) clinical outcomes in NICE 3 were comparable to those in prior studies; 4) it is not necessary to use UF heparin in ACS patients undergoing PCI who are treated with enoxaparin and a IIb/ IIIa antagonist. NICE 3 establishes a strong foundation for future definative large scale randomized efficacy trials.

1253-98 Glycoprotein IIb/IIIa Inhibitors in the Medical Management of Unstable Ischemic Syndromes Without Persistent ST Segment Elevation: A Meta-Analysis of the Randomized Trials

Marco Roffi, Derek P. Chew, Debabrata Mukherjee, Deepak L. Bhatt, Mark A. Robbins, Eric J. Topol. *Cleveland Clinic Foundation, Cleveland, OH*

Background: The role of intravenous glycoprotein (GP) IIb/IIIa receptor inhibitors in the setting of unstable ischemic syndromes without persistent ST-segment elevation treated medically has recently become controversial. So far six placebo-controlled trials have been performed in this setting. **Methods:** PRISM, PRISM PLUS, PARAGON A, PURSUIT, PARAGON B, and GUSTO IV ACS enrolled a total of 29,855 patients. We performed a meta-analysis of these trials and addressed the incidence of death or myocardial infarction (MI) at 30 days. The analysis included all patients enrolled in the trials. **Results:** The results are reported in the figure. The pooled incidence of death or MI at 30 days was significantly reduced by the use of GP IIb/IIIa inhibitors: 10.7 % of the GP IIb/IIIa inhibitor's treated patients and 11.5 % of the placebo treated patients had an event (OR 0.924; 95% CI 0.859-0.995; p=0.037). The p-value of the Breslow-Day test was 0.339, excluding heterogenity of the trials.



Conclusions: The meta-analysis of the so far performed placebo-controlled trials demonstrates that the use of GP IIb/IIIa inhibitors was associated with a modest (8%) but significant reduction in death or MI at 30 days in patients with unstable ischemic syndromes without persistent ST-segment elevation treated medically.

1253-99 Lack of Beneficial Effect of Intravenous Glycoprotein IIb/IIIa Platelet Receptor Inhibitors in Patients With Acute Coronary Syndromes: Time to Reconsider Their Routine Use and Need for a Mortality Trial

Udho Thadani, Saihari Sadanandan. *University of Oklahoma Health Sciences Center, Oklahoma City, OK*

Background: Intravenous (IV) Glycoprotein IIb/IIIa inhibitors (GP IIb/IIIa) are being routinely used in addition to aspirin and unfractionated heparin in the management of pts with non-ST elevation acute coronary syndromes (ACS), who are considered to be at high risk (ACS with ST depression on the EKG and/or positive serum markers). Routine use of this class of drugs has been justified on the basis of their effect on combined endpoint of death and myocardial infarction (MI). However, two recent large trials with these agents have failed to demonstrate a significant benefit on the end points of death and MI. **Methods:** We reviewed data on Death, MI, and major bleeding complications at 30 days from large trials on ACS involving various IV GP IIb/IIIa inhibitors which have been either published or formally presented at major meetings. **Results:**

Trial	Death (%)	p-value	MI (%)	p-value	Severe Bleeding (%)	p-value
PURSUIT						
Eptifibatide	3.5		12.6		1.5	
Placebo	3.7	0.53	13.5	0.14	0.9	<0.001
PRISMPLUS						
Tirofiban	3.6		6.6		4.0	
Placebo	4.5	0.36	9.2	0.05	3.0	0.34
PARAGONB						
Lamifiban	2.9		8.8		1.3	
Placebo	3.3	NS	9.8	NS	0.9	NS
GUSTO ACS						
Abciximab 24h	3.4		5.6		0.6	
Abciximab 48h	4.2		5.9		1.0	<0.001
Placebo	3.9	NS	5.1	NS	0.3	

None of these trials independently showed a reduction in 30-day mortality with the use of any of these agents. Only one study (PRISM-PLUS) showed a reduction in the incidence of MI at 30 days. However the definition of MI in these trials has varied making it difficult to evaluate this endpoint. An increased risk of major bleeding was observed with all these agents and the incidence was statistically signifcant in two of the four clinical trials. In addition, the drug was discontinued due to bleeding more often in PRISM-PLUS trial compared to placebo (3.5% vs. 1.3%, p=0.004). **Conclusions:** IV GP IIb/IIIa inhibitors do not seem to have a beneficial effect on 30-day mortality in pts with ACS, but may increase the risk of bleeding complications. The gold standard for efficacy of thrombolytic agents in pts with ST elevation MI has been their effect on mortality. Before IV GP IIb/IIIa inhibitors can be routinely used in a similar fashion in pts with ACS, their beneficial effect on mortality must be proven in large adequately powered mortality trials.

1253-100 Laser Angioplasty in Acute Ischemic-Thrombotic Coronary Syndromes

On Topaz, Rakesh K. Shah, Robert H. McQueen, Pratik Desai, Yves Janin, Alexandra J. Lansky, Marc E. Carr, Nelson L. Bernardo. *Medical College of Virginia, Richmond, VA*

Background: Patients(pts) presenting with ischemic coronary syndromes oftentimes need mechanical removal of the occlusive thrombus. Thrombi avidly absorb laser energy in the ultraviolet (excimer; 308nm) wavelength. We report analysis of acute results of excimer laser coronary angioplasty (ELCA) in pts presenting with acute thrombotic-ischemic syndromes, i.e.: acute myocardial infarction (AMI) and unstable angina (UA). **Methods:** Fifty-nine pts presenting with acute coronary syndromes were treated with percutaneous ELCA (308nm wavelength, 45mJ/mm^2,25Hz) including 33 pts (39 lesions) with unstable angina (UA) and 26 pts (29 lesions) with AMI. 88% of AMI pts underwent stent implantation versus 76% UA (p=ns). Q.C.A. was performed at an independent core laboratory.

Results: A reduced left ventricular ejection fraction was present in both groups (42±15% AMI vs 49±14% UA, p=ns). 15% of pts with AMI had cardiogenic shock vs 6% for UA (p=0.01). 86% laser success was achieved in the AMI group vs 87% in the UA group (p=ns). Procedural success of 100% was gained in the AMI group vs 97% within the UA group (p=ns). By Q.C.A. analysis MLD increased from 0.8±0.6mm to 1.4±0.5mm post lasing to a final 2.7±0.5 in the AMI group, and from 0.8±0.4mm to 1.4±0.4mm post lasing to 2.7±0.5mm final in the UA group, and pre-laser stenosis was reduced from 76±17% for AMI vs 70±16% for UA (p=ns), to post laser 52±16% for AMI vs 51±14% for UA (p=ns)to final of 15±17% for AMI vs 12±15% for UA (p=ns). Laser induced a 96% reduction of thrombus burden area at the target lesion in the AMI vs 97% in the UA group (p=ns), accompanied by an increased TIMI 1 to TIMI 3 in AMI vs TIMI 2 to TIMI 3 in UA group. There were no death, CVA, emergency bypass surgery, acute closure, perforation, major dissection or bleeding complications in either group. One UA patient had abnormal CPK rise. All 59 pts survived the procedure and were discharged.

Conclusions: In selected pts who present with acute thrombotic-ischemic coronary syndromes, application of excimer laser for thrombus removal and plaque debulking is feasible and safe. Significant laser-induced reduction of thrombus burden occurs.

ORAL CONTRIBUTIONS

871 Regulation of Angiogenesis in Myocardial Ischemia and New Models

Tuesday, March 20, 2001, 4:00 p.m.-5:00 p.m.
Orange County Convention Center, Valencia D

4:00 p.m.

871-1 Classic Ischemic Preconditioning Promotes Myocardial Angiogenesis: Unique Approach to Enhance Contractile Functional Reserve in Rat With Myocardial Infarction

Shoji Fukuda, Genbu Yamaura, Li Zhu, Dipak K. Das, Nilanjana Maulik. *Department of Surgery, University of Connecticut Medical Center, Farmington, CT*

Background: A recent therapeutic approach for treating myocardial ischemia is to induce neovascularization of the heart by use of angiogenic mediators. However, ischemia itself is known to induce angiogenesis. Here we report the ability of a preconditioning stimulus in the form of in vivo brief repetitive cycles of coronary artery occlusion followed by short duration of reperfusion repeated 4 times (4xPC,ischemic preconditioning[IP]) to stimulate myocardial angiogenesis at the capillary and arteriolar levels, assess the functional relevance of such neovascularization by examining the contractile functional reserve as well as blood flow (BF) using radioactive (141Ce) microsphere injection in the rat myocardium after myocardial infarction (MI). **Method:** 120 rats were divided into 4 groups: Control+sham surgery (CS) , control+LAD occlusion (CMI) , 4xPC+sham surgery (IPS) , 4xPC+LAD occlusion (IPMI) (n=12). Rats were subjected to pharmacological stress testing 7 days post-op with dobutamine (DOB) infusion at incremental doses and left ventricular dP/dtmax values were recorded. Radioactive microspheres were used to measure relative BF in sham, control and IP groups (n=12) . Capillary density (CD) and arteriolar density (AD) were evaluated 7 days post-op by immunohistochemistry using anti-CD31 and anti-smooth muscle cell-actin, respectively. Western Blot and immunohistochemistry were performed to measure the protein expression level of vascular endothelial growth factor (VEGF) (n=6) . **Results:** dP/dtmax after DOB infusion was significantly better preserved in the IPMI in comparison to the CMI (6733.5±84.9vs4458.0±181.0mmHg/s) after 7 days. CD as well as AD in IPMI were also significantly increased when compared to the CMI. The rate of BF was increased in the IPMI compared to the CMI. The protein expression level of VEGF in IPMI demonstrated significant upregulation compared to CMI. **Conclusion:** The results indicate first time that IP stimulates VEGF an important mediator of angiogenesis and such stimulation possesses considerable functional relevance in the post-MI state as evidenced by enhanced preservation of contractile functional reserve in a progressing heart failure *model.*

4:15 p.m.

871-2 Vascular Endothelial Growth Factor in Myocardium During Occlusion and Reperfusion

Bo-Qing Zhu, Yi-Ping Sun, Richard E. Sievers, Randall J. Lee, Kanu Chatterjee, William W. Parmley. *University of California, San Francisco, San Francisco, CA*

Background: Vascular endothelial growth factor (VEGF) is a mediator of developmental and tumor induced angiogenesis. In adult tissue and myocardial cell culture, VEGF is significantly increased by myocardial infarction and hypoxia. However, the effects of a differing time course of occlusion and reperfusion has not been investigated. **Methods:** 54 Sprague-Dawley rats were randomly divided into 18 groups: Sham as a control (each group had sham); Occlusion: 5, 10, and 17 min; with Reflow: 0, 1, and 2 hrs. After anesthesia and midline sternotomy, a reversible snare occluder was placed around the proximal left anterior descending coronary artery. After different durations of occlusion and reperfusion (sham was not occluded), the heart was excised. VEGF proteins in the ischemic and nonischemic LV myocardium were measured by Western blot analysis. VEGF change was expressed relative to control (1.0). **Results:** Compared to controls, VEGF in the ischemic myocardium was significantly increased after 10 and 17 min of occlusion (1.5 and 1.7 fold increase over controls, respectively), and significantly decreased after 1 and 2 hrs of reperfusion. **Conclusion:** VEGF in the ischemic myocardium increased after occlusion and decreased after reperfusion. These data suggest that VEGF level is a sensitive indicator of myocardial ischemia.

VEGF changes

Occlusion	5 min		10 min		17 min	
Myocardium	Ischemic	Nonischemic	Ischemic	Nonischemic	Ischemic	Nonischemic
Reflow 0 hr	1.3±0.2	1.0±0.1	1.5±0.1	1.0±0.1	1.7±0.2	0.7±0.3
P value			<0.05		<0.05	
Reflow	0 hr		1 hr		2 hrs	
Myocardium	Ischemic	Nonischemic	Ischemic	Nonischemic	Ischemic	Nonischemic
Occlusion 10 min	1.5±0.1	1.0±0.1	1.3±0.01	1.4±0.2	0.8±0.01	0.5±0.1
P value			<0.05		<0.05	<0.05

4:30 p.m.

871-3 **Temporal and Spatial Localization of the Angiopoietin-TIE-2 System After Myocardial Infarction in the Rat: Evidence of a Role for Ang-2 in Angiogenesis**

Michael J. B. Kutryk, Reena Sandhu, Krystyna Teichert-Kuliszewska, Michael A. Kuliszewski, Sue Nag, Andrew I. M. Campbell, Duncan J. Stewart. *Terrence Donnelly Heart Center, St. Michael's Hospital, Toronto, ON, Canada, Dept of Neuropathology, University of Toronto Health Network, Toronto, ON, Canada*

Background: Angiopoietin-1 (Ang-1) is a newly described angiogeneic factor that promotes vessel maturation and stabilization. In contrast, (Ang-2) is thought to act as an endogenous antagonist of the endothelial cell receptor TIE-2. We examined the expression of Ang-1, Ang-2 and TIE-2 in a rat myocardial infarction (MI) model.
Methods: Hearts were explanted from male SD rats at 24h, 1 and 6 weeks after ligation of the left coronary artery (n=5-7 animals/group). Sham operated (n=6) and untreated (n=9) animals were controls. In all animals, mRNA expression in the infarct (I), peri-infarct (PI), and non-infarcted (NI) zones was determined using semi-quantitative RT-PCR, normalized to GAPDH mRNA expression and confirmed by Northern and Western blotting, and immunohistochemistry.
Results: At 24h Ang-1 levels were decreased in both the I (56±7%, p=0.01) and PI zones (89±6%, p=0.05) compared with the NI zone, while Ang-2 levels were increased in the I (241±63%, p=0.04) and PI zones (222±56%, p=0.03). At 1 week, the I zone showed persistent decreases in Ang-1 (84±3%, p=0.02) and increases in Ang-2 expression (144±9%, p=0.009), whereas Ang-1 and Ang-2 expression had returned to baseline in the PI zone (91±5% and 94±3%, respectively). At 6 weeks, levels of Ang-1 and Ang-2 were not significantly different from control in both territories. TIE-2 receptors levels remained constant in all areas and time points. Northern and Western blotting paralleled the changes in mRNA expression by RT-PCR. Immunostaining for Ang-1 revealed reduced staining of endothelial cells within the ischemic zone at 24h, whereas intense Ang-2 expression was found associated with infiltrating granulocytes and neo-vessels at time points up to 7 days.
Conclusion: The rat model of MI is associated with profound changes in expression of Ang-1 and Ang-2 in the I and PI zones, which support a role for Ang-2 in the angiogenic response to ischemia.

4:45 p.m.

871-4 **Intramyocardial Levels of Vascular Endothelial Growth Factor (VEGF) Are Reduced in a Porcine Model of Hibernating Myocardium**

Patrick W. Domkowski, Shankha S. Biswas, Luis H. Diodato, Anne M. Pippen, Michael A. Thompson, Kevin P. Landolfo, Brian H. Annex. *Duke University Medical Center, Durham, NC*

Background: Ischemia is known to be a potent stimulus for the upregulation of angiogenic growth factors, such as vascular endothelial growth factor (VEGF). Indeed VEGF is upregulated in animal models of hind limb and myocardial ischemia but these models typically examine time points of ≤ 1 month. Our laboratory utilizes a stable model of hibernating myocardium where later time points may be examined. Therefore, the goal of this study was to examine VEGF protein levels in the myocardium at three months following the onset of myocardial ischemia. **Methods:** Six mini-swine with 90% left circumflex artery (LCX) stenosis and documented hibernating myocardium by positron emission tomography (PET with N13 ammonia) and dobutamine stress echocardiography (DSE) were studied 3 months post-operatively. At sacrifice, 6, 3X3mm samples were harvested from both the circumflex (hibernating myocardium) and septal (control, normal perfusion) areas. VEGF levels were determined using commercially available ELISA kits, which have a sensitivity of 10 pg. **Results:** In all animals, the intramyocardial VEGF levels from the circumflex areas were 1 ± 0.2 pg/ml. Comparatively, the VEGF levels in the septal region were 152 ± 18 pg/ml (p<0.001). **Conclusions:** These data indicate that intramyocardial VEGF protein levels are markedly reduced in hibernating myocardium. The angiogenic effects of growth factors delivered into the myocardium with decreased levels of growth factor, as compared to models with increased levels, needs to be determined.

ORAL CONTRIBUTIONS

878 Stabile Ischemic Syndrome: Mechanistic Insights

Wednesday, March 21, 2001, 8:30 a.m.-10:00 a.m.
Orange County Convention Center, Valencia B

8:30 a.m.

878-1 **Large Brachial Artery Diameter Is Associated With Angiographic CAD in Women: A Report From the NHLBI Women's Ischemia Syndrome Evaluation (WISE)**

Richard Holubkov, Richard H. Karas, Carl J. Pepine, Cheryl R. Rickens, Nathaniel Reichek, William J. Rogers, Barry L. Sharaf, George Sopko, C. Noel Bairey Merz, Sheryl F. Kelsey, Susan P. McGorray, Steven E. Reis. *Cardiovascular Institute, University of Pittsburgh, Pittsburgh, PA*

Background: Modification of atherosclerosis risk factors reduces cardiac event rates in women with and without established coronary artery disease (CAD). Since population-based risk factor modification is costly, noninvasive methods are needed to identify women at high CAD risk who might benefit from aggressive preventive therapy. We hypothesized that large resting brachial artery diameter, a marker of peripheral atherosclerosis measurable by ultrasonography, independently predicts CAD in women.
Methods: Women (n=219, mean age 57 years) with chest pain in the NHLBI Women's Ischemia Syndrome Evaluation underwent B-mode ultrasound measurement of brachial artery diameter at rest and during hyperemic stress (to assess % flow-mediated dilatation [FMD]), quantitative coronary angiography, and risk factor assessment.
Results: Women with angiographic CAD (stenosis≥50%) had significantly larger resting brachial artery diameter than those without CAD (4.02±0.79 vs. 3.60±0.55 mm, p<0.001). Brachial artery diameter was also associated with risk factor profile (p=0.006):

Resting Brachial Artery Diameter (mm; mean±SD) by CAD Risk Profile

Number of CAD Risk Factors					
0 (n=13)	1 (n=22)	2 (n=52)	3 (n=59)	4 (n=41)	5 (n=9)
3.45±0.60	3.58±0.50	3.65±0.67	3.85±0.77	3.98±0.70	3.88±0.93

Factors: age≥65, dyslipidemia, hypertension, smoking history, family history of CAD. Women with missing data excluded from table.

After adjustment for age, body size and CAD risk factors, women with large resting brachial diameters (>4.2mm) had 4.6-fold increased odds (95% CI=1.9-11.5, p=.001) of significant CAD compared to those with small brachial arteries (≤3.7mm). Women with intermediate resting brachial diameters (3.7-4.2mm) had a nonsignificant, 2.1-fold increase in CAD odds (95% CI=0.9-4.7, p=.08). Impaired FMD, the traditional surrogate CAD biomarker, was weakly associated with significant CAD (2.17±6.96 vs. 4.52±9.97% in CAD vs. no CAD, p=0.042).
Conclusions: Large resting brachial artery diameter is independently associated with the presence of significant angiographic CAD in women with chest pain. Therefore, measurement of resting brachial diameter provides a noninvasive method to identify women at high risk for CAD.

8:45 a.m.

878-2 **Patients With Inadequate Coronary Collateral Support Are Resistant to Angiogenic Growth Factors**

Pier D. Lambiase, Richard Edwards, Simon R. Redwood, Clifford A. Bucknall, Michael Webb-Peploe, Prodromos Anthopoulos, Jeremy D. Pearson, Michael S. Marber. *St Thomas' Hospital, KCL, London, United Kingdom, Cardiovascular Biology, New Hunt's House, Guy's Campus, KCL, London, United Kingdom*

The factors causing variation in myocardial collateral development are poorly understood. Inadequate collateral formation may be due to impaired angiogenic growth factor (GF) production or an intrinsic myocardial resistance to GF's. **Methods:** 28 patients (age 63±2yr) with stable angina due to isolated LAD disease underwent 2 balloon inflations of >180s separated by 5 mins reperfusion. Coronary occlusion pressure (Poccl) was measured with an 0.014" pressure wire distal to the balloon. Collateral flow index (CFI) was calculated from simultaneous measurements of coronary sinus (CS) & mean aortic pressure (Ao) (CFI= Poccl-CS/Ao-CS). Blood was collected from CS at baseline. Serum relative mitogenicity (RMit) was determined using a 3H thymidine incorporation assay in both human umbilical artery smooth muscle (HUASMC) & venous endothelial cells (HUVEC) & is expressed relative to standard pooled human serum. Angiogenic potential was assessed in a matrigel assay employing HUVEC. Myocardial ischemia was assessed by the greatest degree of ST shift (mm) recorded from intracoronary and surface ECG during balloon occlusion. **Results:**11 patients had CFI>0.25 (40% ; Group 1) and 17 (60% ; Group 2) had inadequate collateral support; (CFI<0.25). Baseline RMit was 1.7 fold higher in Group 2 (1.9 ±.2 vs 1.1±.1 mean±SE p=0.005) with an inverse correlation between RMit & CFI (r=-0.6 p=0.002). In vitro tube formation was significantly greater in Group 1 (90% of control vs 60% p=0.005). No differences were detected in HUASMC mitogenicity or CS plasma VEGF & FGF levels between the 2 groups. Time to 1mm ST depression during a pre-PTCA exercise ECG was equivalent for each group. However, during PTCA, the degree of ST elevation was 9 fold higher in the CFI <0.25 patients (9.3±.3mm vs 0.8±.4mm p=0.0001). **Conclusions:** Compared to patients with well developed collateral support patients with inadequate collaterals have 1) More mitogenic serum despite similar ischemic burden & 2) Reduced in vitro angiogenic potential. These findings suggest that impaired collateral formation may reflect an intrinsic myocardial resistance to angiogenic GFs.

9:00 a.m.

878-3 **Morbidly Obese Patients Undergoing Cardiac Catheterization: Less Disease, Less Aggressive Revascularization, and Similar Outcomes**

John H. Alexander, Karen P. Alexander, Peter J. Joski, Michael S. Cuffe, Robert H. Peter. *Duke University Medical Center, Durham, NC*

Background: Little is know about cardiac catheterization in the morbidly obese (BMI>40). These patients have a high prevalence of cardiac risk factors but are particularly difficult to study non-invasively and are thus often referred for cardiac catheterization. The Duke Cardiovascular Database, which possibly contains the world's largest database of obese patients undergoing cardiac catheterization, offers a unique opportunity to investigate the characteristics and long-term outcome of this population. **Methods:** The Database includes baseline and angiographic variables and long term survival for all patients undergoing cardiac catheterization at a single institution. We compared extent of coronary artery disease, revascularization rates for those with more than 1 vessel CAD, and survial in morbidly obese patients (BMI>40 and>50) and non-morbidly obese patients (BMI<40) undergoing cardiac catheterization at Duke between 1/1/1986 to 12/31/1999. **Results:** Out of 37,999 patients included in the sample 1304 had a

BMI>40 and 223 had a BMI>50. Obese patients were younger, more likely to be female, of African American race, and to have diabetes, hypertension, and hyperlipidemia but were less likely to be smokers or have previously documented coronary disease.

Results

	BMI < 40	BMI > 40	BMI > 50	P
Weight	173.8	270.6	349.8	<0.001
0 vessel	33.9	53.6	60.8	<0.001
1 vessel	23.7	16.9	11.0	
2 vessel	19.1	15.5	12.7	
3 vessel	23.3	14.0	15.5	
LM (>75%)	5.0	3.0	1.6	
PTCA	29.2	37.7	35.2	<0.001
CABG	32.7	24.4	22.5	<0.001
5/10 yr survival	0.80 / 0.61	0.81 / 0.54		0.668

Conclusion: Dispite being younger and having less severe coronary disease, morbidly obese patients undergoing cardiac catheterization at Duke have similar 5 and 10-year survival. This may represent the impact of morbid obesity on either ischemic or non-ischemic causes of premature death or reflect less aggressive managment of exisiting coronary artery disease.

9:15 a.m.

878-4 **Energy Metabolism of Human Hibernating Myocardium: Implications for Contractile Dysfunction**

Achim M. Vogt, Klaus D. Müller, Woitek Skwara, Jutta Schaper, Christoph Bode, Wolfgang Kübler, Albrecht Elsässer. *Dept. Cardiology, Heidelberg University, Heidelberg, Germany, Dept. Cardiology, Freiburg University, Freiburg, Germany*

Background: In myocardial ischemia, the energy level determines contractile performance. To elucidate the pathomechanisms underlying contractile dysfunction of human hibernating myocardium (HHM), an in-depth analysis of its energy metabolism was performed.

Methods: In 16 patients with documented coronary artery disease and impaired left ventricular function, HHM was identified by thallium 201-scintigraphy, radionuclide ventriculography, and low-dose dobutamine echocardiography, performed preoperatively and three months after revascularization. During open-heart surgery (OP), transmural biopsies were removed from the hibernating areas. Both, metabolite contents (HPLC) and fibrosis (microscopy) were assessed from the same hibernating area, allowing to normalize total myocardial metabolite content to the cellular myocardial fraction (CMF). HHM-data were compared to normal human myocardium (control; n=7).

Results: All patients showed diagnostic concordance of the clinical markers of HHM pre-OP and a significant improvement of regional contractile performance following revascularization. In HHM, total myocardial as well as cellular levels in ATP and phosphocreatine (CP) were reduced (see table), as were energy charge (EC), phosphorylation potential (P-Pot) and the free energy of ATP hydrolysis (ΔG_{ATP}).

High energy phosphate contents and energetic parameters in human hibernating myocardium

		ATP	CP	EC	P-Pot	ΔG_{ATP}
control	total content	3.75±.23	5.11±.63	.96±.02	2.91±.84	-55.9±.89
	CMF	4.17±.26	5.67±.70			
HHM	total content	1.24±.18*	.62±.11*	.73±.03*	.96±.10*	-53.2±.47*
	CMF	1.72±.25*	.85±.13*			

*: p<.005 (ANOVA), metabolite contents in µmol/g wet wt, ΔG_{ATP} in kJ/mol.

Conclusion: This first description of HHM's energy metabolism reveals that HHM is severely energy depleted myocardium. Due to the well established impact of energy metabolism on contractility we suggest that these energetic alterations contribute to HHM's impaired contractile performance.

9:30 a.m.

878-5 **Percutaneous Intervention in Plaques With Increased Temperature is Associated With Unfavorable Outcome in Patients With Effort Angina**

Christodoulos I. Stefanadis, Konstantinos P. Toutouzas, Eleftherios Tsiamis, Manolis Vavouranakis, Ioannis Kallikazaros, Charalambos Vlachopoulos, Athanasios Trikkas, Sophia Vaina, Pavlos K. Toutouzas. *Hippokration Hospital, Athens, Greece*

Background: It has been shown that patients with effort angina have increased temperature of the culprit atherosclerotic plaque. The present study was designed to investigate the significance of temperature measurement of the atherosclerotic plaque in patients with effort angina. **Methods:** Balloon angioplasty was performed in 30 patients, mean age 61.4±8.1 years, with effort angina. We measured the temperature difference (ΔT) between the atherosclerotic plaque and the healthy vessel wall with a thermography catheter previously validated, after accomplishing TIMI III flow. A metallic stent was implanted in all patients. **Results:** All procedures were performed successfully and without complications. In the study population mean ΔT was 0.132±0.18°C. All patients were followed-up for 17.0±5.2 months, during which 4 patients suffered from an adverse cardiac event. Patients with adverse cardiac events had increased ΔT compared to those without events (ΔT:0.07±0.09°C vs. 0.52±0.07°C;C.I [-0.54 - -0.36], P<0.001). The risk for an adverse cardiac event was increased in patients with "hot" plaques (odds ratio 1:41). **Conclusions:** The increased temperature of the culprit atherosclerotic plaques of patients with effort angina, in whom elective percutaneous intervention was performed, is associated with unfavorable clinical outcome.

9:45 a.m.

878-6 **Polymorphisms of Factor V Leiden, Prothrombin e Methylenetetrahydrofolate Reductase in Patients With Coronary Disease**

Antonio P. Mansur, Joyce M. Annicchino-Bizzacchi, José A. F. Ramires. *Heart Institute (InCor), University of São Paulo Medical School, São Paulo, Brazil*

Factor V Leiden, prothrombin 20210A allele and methylenetetrahydrofolate reductase (MTHFR) have been associated with coronary artery disease (CAD) in some studies but not in others. Negative study results were due to the small number of study patients or to single gene analysis in a multifactorial disease. Analysis of a panel of two or more polymorphisms may increase CAD identification. **Methods:** In a case-control study, we analyzed factor V Leiden, prothrombin 20210G/A mutation and 677C->T mutation of methylenetetrahydrofolate reductase (MTHFR) in 368 patients with CAD and 368 control subjects matched by age, sex, and race. Gene polymorphisms were determined by the polymerase chain reaction. Panels were constructed of two or three polymorphisms previously associated with CAD. **Results:** Factor V Leiden mutation was higher in patients with CAD (4.4% vs 0.8%; p=0.003), in men with CAD (4.6% vs 0.4%; p=0.004), in patients ≤ 45 years (4.8% vs 0%; p=0.032), or > 45 years (4.2% vs 1.2%; p=0.036). Polymorphisms were not associated in women with CAD. A panel of two polymorphisms that included factor V Leiden mutation was associated with CAD. Multivariate analysis disclosed factor V Leiden as an independent variable for CAD [OR=4.4 (CL95%: 1.2-16.7; p=0.02)]. **Conclusion:** Of all polymorphisms, only factor V Leiden was shown to be an independent marker for CAD. The panel of two or more polymorphisms did not increase CAD identification.

ORAL CONTRIBUTIONS

879 Advances in the Pharmacotherapy of Acute Myocardial Infarction

Wednesday, March 21, 2001, 8:30 a.m.-10:00 a.m.
Orange County Convention Center, Room 231A

8:30 a.m.

879-1 **Is IIb/IIIa Blockade State-of-the-Art for Catheter Based Reperfusion? A Meta-Analysis of Five Randomized Trials in Acute Myocardial Infarction**

Umesh N. Khot, Franz-Josef Neumann, Sorin J. Brener, Albert Schomig, Gilles Montalescot, Shelly Sapp, Eric J. Topol. *The Cleveland Clinic Foundation, Cleveland, OH*

Background: Glycoprotein IIb/IIIa inhibitors have been shown to improve clinical outcomes in patients with unstable and stable angina undergoing various types of percutaneous intervention. Whether there is a similar benefit in patients undergoing percutaneous intervention for acute myocardial infarction is not established.

Methods: To address this issue we performed a meta-analysis of 1369 patients from five randomized clinical trials (EPIC, RAPPORT, ISAR-2, ADMIRAL, and STOPAMI) of abciximab in percutaneous intervention for acute myocardial infarction. We compared clinical outcomes in 684 patients who received abciximab with 685 patients who did not receive abciximab.

Results: Abciximab caused a significant 43% reduction in the incidence of both death and myocardial infarction at 6 month followup (P=0.003).

Conclusion: When used in percutaneous intervention for acute myocardial infarction, abciximab use led to a pronounced reduction in mortality and furthermore decreased the incidence of recurrent myocardial infarction. This benefit was apparent at 30 day followup and was more pronounced at 6 month followup.

Aggregate Data from 5 Randomized Trials

	Abcix-imab	No Abciximab	Odds Ratio	95% Confi-dence Interval	P Value
30 Day Death	2.8%	4.2%	0.65	0.36 - 1.16	0.141
30 Day Death/Myocardial Infarction	4.2%	7.2%	0.57	0.36 - 0.92	0.02
6 Month Death	4.2%	6.7%	0.61	0.38 - 0.98	0.043
6 Month Death/Myocardial Infarction	7.0%	11.7%	0.57	0.39 - 0.83	0.003

8:45 a.m.

879-2 **Aspirin Plus Medium Intensity Coumadin Versus Aspirin Alone in the Prevention of Reocclusion After Successful Thrombolysis for Suspected Acute Myocardial Infarction: Results of the APRICOT-2 Trial**

Marc A. Brouwer, Paul J. P. C. van den Bergh, Ralf P. J. W. Vromans, Wim R. M. Aengevaeren, Gerrit Veen, Hans E. Luijten, Don P. Hertzberger, Ad J. van Boven, Gerard J. H. Uijen, Freek W. A. Verheugt. *Heartcenter, University Medical Center, Nijmegen, The Netherlands, Interuniversity Cardiology Institute Netherlands, Utrecht, The Netherlands*

Background: Within a year after successful thrombolytic therapy reocclusion of an infarct related artery occurs in about 30% of patients, despite the use of aspirin. It is associated with an increased risk of death and reinfarction, and has been reported to preclude left ventricular contractile recovery. **Methods:** The APRICOT-2 trial (Antithrombotics in the Prevention of Reocclusion In COronary Thrombolysis) is a multicenter, randomized,

clinical and angiographic follow-up study: 308 patients (< 76 years) received thrombolytic therapy for signs and symptoms of suspected acute transmural myocardial infarction within 6 hours of onset, and showed TIMI 3 flow at coronary angiography performed within 48 hours after thrombolysis. Thereafter, they were randomized to either aspirin 80 mg daily, or to the combination of aspirin 80 mg and medium intensity Coumadin (target INR: 2-3). Follow-up angiography was scheduled at three months. **Results:** Reocclusion rate (< TIMI 3 flow) was 30% for patients on aspirin, compared with 18% for those on combination therapy (RR 0.60; CI 0.39 – 0.93; p = 0.02). Patients on aspirin showed TIMI 0-1 flow in 19% of patients, compared with 11% for those on aspirin and Coumadin (RR 0.52; CI 0.28 – 0.96; p = 0.03). Death and/or reinfarction were seen in 7% and 3% of patients, respectively (RR 0.38; CI 0.12 - 1.20; p = 0.09). **Conclusions:** These findings strongly suggest that the combination of aspirin with medium intensity Coumadin markedly reduces clinical and angiographic reocclusion after successful thrombolysis for suspected acute myocardial infarction. Adjudicated trial data and 1 year follow-up will be presented.

9:00 a.m.

879-3 Early Statin Treatment Improves Long-Term Survival in Patients Discharged Alive After Acute Myocardial Infarction

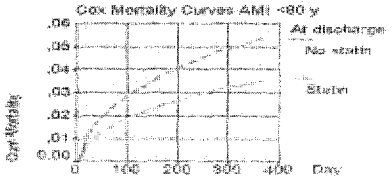
Ulf Stenestrand, Lars Wallentin, the RIKS-HIA group. *Heart Center, University Hospital, Linkoping, Sweden, Dept of Cardiology, University Hospital, Uppsala, Sweden*

Background: Randomized trials have shown that statin treatment is beneficial as secondary prevention in patients with cardiovascular disease. It is still unclear if statin treatment started already in hospital will influence long-term outcome. Furthermore it is also unknown how results from randomized trials translate into effects in an unselected patient population. We investigated the effect of early statin treatment on one-year survival in an large cohort of consecutive unselected acute myocardial infarction (AMI) patients.

Methods: From the Swedish Register of Cardiac Intensive Care, which included every CCU admitted patient at 58 participating hospitals 1995-98, the 20,547 AMI patients <80 years old who were alive at discharge were included in the analyses. Cox regression analysis was performed evaluating the effect of statin treatment initiated before or at discharge regarding one-year mortality taking into consideration 26 factors known to influence survival such as clinical background, medication, interventions and complications.

Results: In the 14,752 patients without statin treatment the unadjusted one-year mortality was 9.4% (1,385) compared to 4.1% (235) in the 5,795 patients on early statin treatment. In Cox regression analysis adjusting for the 26 covariates early statin treatment was associated with a risk reduction of 35% for one-year mortality RR 0.65 (95% CI 0.55-0.77), p<0.001.

Conclusion: Early initiated statin treatment in AMI patients significantly reduces one-year mortality. Furthermore this register study shows that the results from randomized statin trials will have important implications also when transferred to an unselected AMI population



9:15 a.m.

879-4 Lmw Heparin (Dalteparin) for Improvement of Patency After Thrombolysis in AMI: A Prospective Randomized Multicentre Coronary Angiography Study

Mikael Dellborg, Lott Bergstrand, Chris Granger, Bertil Lindahl, Tage Nilsson, Kenneth Persson, Eva Pihl, Agneta Siegbahn, Eva Swahn, Lars Wallentin, The ASSENT PLUS Investigators. *Dept. of Medicine, Sahlgrenska University Hospital/Ostra, Göteborg, Sweden, Uppsala University, Uppsala, Sweden*

Background: Despite improvement of 60 minutes coronary blood flow there are no added benefits in clinical outcome by the new fibrinolytic agents. This might be caused by reocclusion during and after the associated 48-hour heparin infusion. The primary aim of the present trial was to evaluate whether s.c. dalteparin until a coronary angiogram after 4 – 7 days is more effective than 48-h heparin infusion in obtaining patency and TIMI-3 flow after thrombolysis with rt-PA in acute myocardial infarction (AMI).

Methods: Patients with an AMI and an indication for thrombolysis within 6 h of symptom onset were openly randomised to heparin infusion for 48 h or i.v. bolus followed by s.c. dalteparin 120 IU/kg every 12 h until coronary angiography after 4 – 7 days. All coronary angiograms were centrally and blindly evaluated concerning TIMI flow grade (1^0 objective). Other objectives were safety, noninvasive signs of early reperfusion , coagulation and bleeding parameters, clinical events during treatment (max. 7 days) and 30 days

Results: 439 patients, mean age 65 yrs, 70% male, were randomised in 18 Swedish and 4 U.S. hospitals , 378 performed per protocol angiography.

	Dalteparin	Standard heparin	p
TIMI-3 flow (n=202/176) (%)	69.3	62.5	0.16
Visible thrombus (n=202/176) (%)	18.9	27.3	0.054
TIMI 2/3 + no thrombus (n=202/176) (%)	72.1	58	0.004
Reinfarction until 7 days (n=216/204) (%)	1.4	5.4	0.02

At 30 days, no significant differences in death, reinfarction or revascularization were observed. No significant differences were observed in bleeding or other side-effects.

Conclusion: The combination of bolus tPA agents and bolus i.v. followed by s.c. dalteparin was related to fewer coronary occlusions, a lower incidence of coronary thrombus and fewer reinfarctions during the first 7 days compared to standard heparin. This was observed without any increase in bleeding events. Possibly due to rebound after cessation of dalteparin, no difference in clinical outcome was observed at 30 days. Confirmation of these findings in larger studies is warranted.

9:30 a.m.

879-5 Therapeutic Margin of Safety With Weight-Optimized Dosing of Tenecteplase

Brad G. Angeja, Richard Chin, Xin Li, Hal V. Barron, Christopher Granger, Frans Van de Werf, C. Michael Gibson. *University of California, San Francisco, Duke Clinical Research Institute, Durham, NC*

Background: The Assessment of Safety and Efficacy of a New Thrombolytic (ASSENT)-2 trial demonstrated that tenecteplase (TNK) is equivalent to alteplase (tPA) for treatment of myocardial infarction using weight-optimized doses, and we sought to evaluate the safety of errors in weight-optimized dosing. **Methods:** Rates of intracranial hemorrhage (ICH) and death were determined 1) among all patients treated with the highest dose (50 mg) of TNK; 2) among patients weighing < 90 kg who received 50 mg TNK in error; and 3) among all patients receiving any incorrect dose of TNK. **Results:** 1) A total of 1,915 patients received 50 mg TNK, whom we compared to 1,919 tPA patients weighing > 90 kg (control group matched for weight). The rate of ICH with 50 mg TNK (0.57%) was similar to that with tPA (0.47%, P = 0.65), as was the rate of death (4.70% vs. 3.96%, P = 0.26). Multivariate adjustment did not change these results (P = 0.21 for both). 2) Of patients receiving 50 mg TNK, 150 (7.8%) weighed < 90 kg as specified by the protocol and received an excess dose of TNK in error. Rates of ICH (1.33%) and death (6.67%) were not significantly different than those among patients < 90 kg who received other thrombolytic doses (ICH = 1.06%, P = 0.68; death = 6.66%, P =1.00). 3) Of all patients given TNK, 218 patients (2.7%) received doses greater than recommended, and 326 (4.0%) received doses less than recommended. The median weight error in overdose was 8 kg and in underdose was 1 kg. Neither underdosing nor overdosing of 1 - 2 dosing intervals (up to 20 Kg or 44 pounds in error) was associated with ICH (odds ratio = 0.63 [P = 0.53] & 1.00 [P = 1.00], respectively) or death (OR = 1.09 [P = 0.73] & 0.84 [P = 0.64], respectively) in a multivariate model accounting for weight. **Conclusions:** In this limited sample, there were no obvious differences in the rates of ICH and death with dose errors of TNK compared to rates among weight-matched controls treated with the correct dose. While correct dosing remains the goal, there appears to be an acceptable margin of safety with errors in weight-optimized dosing of TNK.

9:45 a.m.

879-6 Protection of Left Ventricular Function with Recombinant Soluble P-Selectin Glycoprotein Ligand-Ig in the Canine Coronary Balloon Occlusion Model

Kai Wang, Zhongmin Zhou, Xiaorong Zhou, Khaldoun Tarakji, Jian Xin Qin, Marta Sitges, Marta Sitges, Takahiro Shiota, Eric Topol, A. Michael Lincoff. *The Cleveland Clinic Foundation, Cleveland, OH*

Background: Recombinant P-selectin glycoprotein ligand-Ig (rPSGL-Ig) is a soluble form of high-affinity counterreceptor for P-selectin. Its effect on left ventricular function after AMI was evaluated in a canine ischemia-reperfusion model.

Methods: A balloon-occluded model was used in this study. LAD occlusion was achieved using balloon inflation for a total of 90 minutes in 10 hound dogs (20-22kg) (rPSGL-Ig=5, placebo=5). rPSGL-Ig (1mg/kg) or saline was given as a bolus intravenously 15 minutes before reperfusion. All animals were followed for one week. Real-time 3-dimensional echocardiography was used to evaluate the left ventricular function.

Results: Infarct size was significantly reduced in the treatment group when expressed either as percentage of the area at risk (rPSGL-Ig, 7.19±7.27%; placebo, 21.80±5.41%; p=0.007) or as absolute infarct size (Table). Left ventricular function expressed as ejection fraction (EF) was much improved at 2 hours after reperfusion (rPSGL-Ig, 43.3±4.13%; placebo, 28.48±8.07%; p=0.017), however, at 1 week follow-up this difference was no longer significant due to recovery of the placebo group (rPSGL-Ig, 47.55±10.85%; placebo, 45.54±5.00%; p=0.781).

Table. Myocardial Area at Risk and Effects of rPSGL-Ig on Infarct Size

	Placebo	rPSGL-Ig	P value
Area at risk, cm^2	53.14±8.95	52.55±6.14	NS
Infarct size, cm^2	12.01±2.80	3.90±4.39	0.008

Conclusion: The administration of rPSGL-Ig results in significantly improved left ventricular function in the early time period after AMI through salvage of jeopardized myocardium.

ORAL CONTRIBUTIONS

883 New Horizons for Surgical Myocardial Revascularization

Wednesday, March 21, 2001, 8:30 a.m.-10:00 a.m.
Orange County Convention Center, Room 304A

8:30 a.m.

883-1 Prospective Ten-Year Patency of Saphenous Vein and Left Internal Mammary Artery Grafts After Coronary Artery Bypass Surgery

Steven Goldman, Karen Zadina, Thomas Moritz, Theron Ovitt, Gulshan Sethi, Jack Copeland, William Henderson, VA Cooperative Study #364. *Southern Arizona VA Healthcare System, Tucson, AZ, Edward Hines, Jr., VA Hospital, Hines, IL*

Background: This Department of Veterans Affairs Cooperative registry prospectively defined long term saphenous vein graft (SVG) and left internal mammary artery (IMA) graft patency in patients undergoing coronary artery bypass grafting (CABG) in the late 1980s.
Method: As part of an ongoing trial, we obtained serial angiographic data at one week, one year, three years, and ten years after CABG. Initially, 1196 patients were enrolled in the trial. At ten years, we obtained angiographic data on 365 patients, while 441 patients had died, and 390 patients did not undergo angiography.
Results: The SVG and IMA patency rates at ten years were 65.8% and 90.4%, respectively. If a patient had a patent SVG or IMA at one week, that graft had a 72.2% and 92.8% chance, respectively, of being patent at ten years. For SVGs, the first year patency rate was 82.4%, three-year patency was 77%, and ten-year patency was 65.8%. For IMA grafts, the first year patency rate was 94.9%, three-year patency was 90.5%, and ten-year patency was 90.4%. There was a significant difference between the patency rates by location (p<0.05). At ten years, the SVG patency of the left anterior descending was better (70.7%) than that of the right coronary artery (60.5%). There was no significant difference in patency rates between the left anterior descending and the circumflex (64.9%).
Conclusions: Our conclusion is that when prospective angiographic follow-up are obtained on patients undergoing CABG in the 1980s, the long-term patency for SVGs is better than previously thought. For SVGs, the most important predictor of long-term graft patency is patency at one week after CABG.

8:45 a.m.

883-2 Minimal Invasive Bypass Surgery Versus Stentimplantation in Isolated Proximal High Lesions of the LAD in More Than 200 Patients

Holger Thiele, Anno Diegeler, Bernward Lauer, Rainer Hambrecht, Friedrich W. Mohr, Gerhard Schuler. *University of Leipzig, Heart Center, Leipzig, Germany*

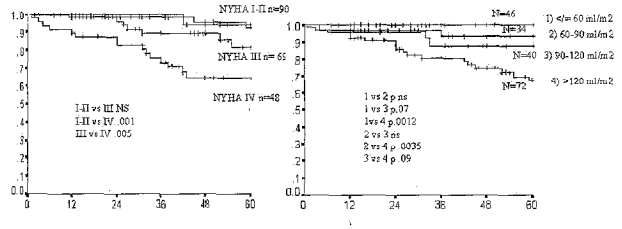
Background: Minimal invasive bypass surgery (MIDCAB) has been shown to yield comparable results to conventional bypass grafting with less operative trauma. Therefore it may be considered an alternative treatment to stentimplantation in patients with proximal high-grade lesions of the LAD. **Methods:** 220 patients with high-grade lesions of the proximal LAD were randomized between MIDCAB (110) and stentimplantation (110). Clinical symptoms were assessed by CCS-class. After 6 months patients underwent repeat coronary angiography. **Results:** During MIDCAB 4 patients (4%) were converted to conventional bypass surgery and 2 patients required repeat operation due to stenosis of the distal anastomosis within 1 week. Acute stent thrombosis occurred in 2 P (2%). After 6 months 33/97 patients (34%) in the stent group showed in-stent restenosis >50% of who 26 (27%) underwent re-PTCA. In the MIDCAB-group 13/91 (16%) showed stenosis >50% of the distal anastomosis, 5 patients (6%) required PTCA (p=0.02). Relieve of angina at 6 months was more complete at 6 months in MIDCAB as compared to stentimplantation (CCS 0.3±0.6 vs. 0.7±1.0; p<0.001), although physical work capacity did not differ between the groups (p=n.s.). Subgroup analysis showed no differences for type A, B, C stenoses or patients with diabetes mellitus after MIDCAB or stentimplantation. **Conclusions:** In patients with high-grade lesions of the proximal LAD both MIDCAB and stentimplantation yield excellent results, although MIDCAB is associated with a higher rate of periprocedural events. After 6 months the reintervention rate is higher in the stent group and symptomatic relieve is more complete after MIDCAB.

9:00 a.m.

883-3 Efficacy of Dor Procedure on Late Survival in Patients With Postinfarction Akinetic or Dyskinetic Scar and Predictors of Outcome

Marisa Di Donato, Michel Sabatier, Anna Toso, Mauro Maioli, Vincent Dor, Gian Franco Gensini, Gerald Buckberg. *Dpt of Critical Care Medicine, Florence, Italy, Cardio Thoracic Center, Monaco, Monaco*

Background: Dor procedure is a surgical technique consisting in endoventricular patch plasty repair (EVCPP) of the left ventricle (LV) and associated coronary grafting, that applies to postinfarction pts with either akinesia or dyskinesia and LV pump dysfunction. **Methods:** This study examined the effects of this procedure on long term survival and the association with preoperative clinical and hemodynamic variables in 207 consecutive surviving patients (perioperative mortality 7.9%) submitted to EVCPP at the Cardiothoracic Center of Monaco during 4 years activity. Mean age was 58±8 yrs; delay from MI: 42±52 m; EF: 35%±12. **Results:** There were 27 late deaths and 3 heart transplantation during follow up (45±27months). Causes of death included CHF in 16, sudden death in 8 and non cardiac in 3. Preoperatively, 117 out of the 207 (57%) were in NYHA class III-IV, 80 pts (39%) had an EF less than 30% and 72 patients (35%) had an ESVI greater than 120 ml/m2. For these patients late mortality rate was 21%, 26% and 28%, respectively. Graphic shows Kaplan Meyer survival curve in patients divided by preoperative end systolic volume index and NYHA class. Perioperative deaths are excluded. At Cox regression analysis predictors of late deaths were preoperative left ventricular volumes, ejection fraction, NYHA class and the presence of remote asynergy (p <0.0000). **Conclusion:** Dor procedure has a favorable impact on survival in postinfarction patients with severe LV dysfunction and high functional class. Predictors of late deaths are severe clinical conditions and pump dysfunction and this suggests that an earlier intervention might further improve survival.



9:15 a.m.

883-4 Correlation of NOGA™ Left Ventricular Electromechanical Mapping and Radionuclide Perfusion Imaging Demonstrating Augmented Perfusion of Ischemic Myocardium in Patients Undergoing Direct Myocardial VEGF-2 Gene Transfer

Peter R. Vale, Charles E. Milliken, David Fortuin, Richard A. Schatz, Maria C. McDonald, Darryl D. Esakof, Michael Maysky, Alan B. Ashare, James F. Symes, Jeffrey M. Isner, Douglas W. Losordo. *St Elizabeth's Medical Center, Boston, MA, Scripps Clinic, La Jolla, CA*

Background: We present the combined results of NOGA™ left ventricular (LV) electromechanical mapping (EMM) and radionuclide perfusion imaging in pts undergoing direct myocardial gene transfer (GT) with naked DNA encoding for vascular endothelial growth factor-2 (phVEGF-2). **Methods:** A total of 16 pts (14 men, mean age 62.3±2.3 yrs) with non-revascularizable chronic stable angina underwent SPECT-Sestamibi imaging and EMM prior to direct myocardial injection of phVEGF-2 via mini-thoracotomy, receiving doses of 200µg (n=7), 800µg (n=4) and 2000g (n=5) as part of a multicenter, open labelled, non-randomized clinical trial. Foci of ischemic myocardium were identified on EMM by preserved viability (unipolar (UpV) and bipolar (BpV) voltage recordings >=5mV and >=2mV respectively) associated with an impairment (<12%) in linear local shortening (LLS). A 20-segment scoring system was used to calculate stress and rest perfusion scores. **Results:** Myocardial segments with normal radionuclide perfusion (n=195) had normal LLS (pre-GT=12.2±0.7 vs post-GT=13.8±0.8%), and normal UpV (12.4±0.8 vs 13.3±0.6mV) and BpV (3.2±0.3 vs 3.5±0.3mV). Segments with reversible ischemia and normal resting perfusion (n=37) showed improved LLS (7.4±1.3 vs 14.2±0.9%, p<0.001) associated with reduced (i.e improved) stress score (4.5±1.2 vs 2.4±0.9, p=0.005) post-GT. This correlated with reduced area of ischemic myocardium (7.8±1.5cm2 vs 3.1±1.4cm2 p=0.0001). Segments with resting perfusion defects (n=92) had ischemic LLS and normal voltages pre-GT, but showed normalization of LLS (8.7±0.7 vs12.0±0.6%, p<0.001) post-GT, while UpV (12.5±0.8 vs 12.1±1.1mV) and BpV (4.0±0.4 vs 3.4±0.4mV) remained unchanged. Conversely, ischemic segments on EMM (n=77) had improved stress (9.3±2.4 vs 5.4±1.6, p=0.019) and rest (6.2±1.6 vs 3.6±1.1, p=0.027) perfusion scores post-GT. **Conclusions:** The results of EMM constitute objective evidence that phVEGF-2 GT augments perfusion of ischemic myocardium and correlates with findings on Sestamibi imaging. Resting perfusion defects may constitute areas of hibernating myocardium that can be successfully revascularized by therapeutic angiogenesis.

9:30 a.m.

883-5 Perioperative Antioxidant Treatment With Vitamin C Reduces the Incidence of Atrial Fibrillation After Coronary Artery Bypass Surgery

Mina K. Chung, Barbara Elias, Stephen Pavia, Cynthia A. Carnes, Patrick M. McCarthy, David R. Van Wagoner. *The Cleveland Clinic Foundation, Cleveland, OH*

Cardiac surgery can cause ischemic or reperfusion injury, which can produce free radicals acutely, during reperfusion or during later inflammatory phases. We hypothesize that the oxidative stress associated with cardiac surgery has a direct negative impact on electrophysiologic properties of the atria. The response to this oxidative stress depends on the antioxidant capacity of the patient. To test this hypothesis, we evaluated the impact of vitamin C (VitC) treatment on the incidence of postoperative atrial arrhythmias (AF). **Methods:** In a pilot series of 50 sequential patients undergoing primary CABG with normal renal function and in sinus rhythm, VitC 2 g the night before CABG and 500 mg bid x5 days postoperatively was prescribed. This series was compared to an age- and gender-matched Control group that underwent CABG the 6 weeks following the pilot study. **Results:** Age (61.8±11.1 Control vs 61.7±12.1 VitC) and LVEF (48.6±10.9% Control vs 49.7±11.1% VitC, p=ns) were similar between groups. Postoperative AF developed in 6/43 (14.0%) patients pretreated with VitC, compared to 14/43 (32.6%) in the control group, p=0.041. Significant univariate predictors of postoperative AF included older age (p=0.006) and LVEF (P=0.021), but additional postoperative beta blocker use in the VitC patients and off-pump CABG did not confer additional reduction in AF. Multivariable logistic regression analysis identified VitC pretreatment (odds ratio OR 0.237, 95% CI 0.0678-

0.829, p=0.024), age (OR 1.087, 95% CI 1.027-1.151, p=0.004), and LVEF (OR 0.937, 95% CI 0.890-0.986, p 0.012)as independent factors associated with postoperative AF with Vitamin C having a protective effect. **Conclusions:** Vitamin C may reduce the incidence of atrial fibrillation by more than half after CABG. Additional randomized, blinded studies are needed to confirm and extend this finding.

9:45 a.m.

883-6 Robotically Assisted Cardiac Surgery: The Dresden Experience

Romuald Cichon, Utz Kappert, Jens Schneider, Ina Schade, Vassilios Gulielmos, Sems Malte Tugtekin, Klaus Matschke, Stephan Schueler. *Cardiovascular Institute, University of Dresden, Dresden, Germany*

Background: The consequent development of minimally invasive techniques in coronary artery surgery, focussing on the avoidance of median sternotomy, has lead to a differentiated therapeutical concept for the treatment of patients suffering from coronary artery disease (CAD). With the introduction of the da Vinci™ robotic surgical system (Intuitive Surgical) into minimally invasive cardiac surgery the outlook of performing coronary artery bypass operations 'closed chest' became a reality. **Methods:** Between 5/99 and 6/00 this new wrist-enhanced instrumentation was used in 134 patients (100 male, 34 female, median age 63 ± 10.1 years). Twelve patients suffering from single vessel CAD and one patient suffering from double vessel CAD were treated as totally endoscopically coronary artery bypass (TECAB). Seventy-three patients with single vessel CAD underwent a minimally invasive direct coronary artery bypass procedure. Thirty-two patients with double vessel CAD were treated using the robotic-enhanced Dresden Technique. Sixteen patients received a median sternotomy: Seven patients necessitated an intraoperative conversion to a median stenotomy. Nine patients received robotic-assisted coronary artery bypass grafting via a median sternotomy already preoperatively planned. **Results:** Perioperative survival was 100%. Internal mammary arteries (IMA) were always harvested totally endoscopically except in four patients. All IMA´s had excellent flow. All patients out of the TECAB group were operated upon via a three or four point stab incisions using the da Vinci™ robot for left IMA or bilateral IMA takedown and for performance of anastomoses. The time of dissection of the left IMA could be significantly reduced. In the TECAB group all patients were operated upon via a three (TECAB) or four (beating heart TECAB) point stab incisions. Preoperative, perioperative, and postoperative data were observed. **Conclusions:** Our preliminary experiences with this new surgical techniques for robotic-enhanced minimally invasive treatment of CAD promote an optimistic way of thinking about the further development of these procedures and its application in patients suffering from CAD.

POSTER SESSION

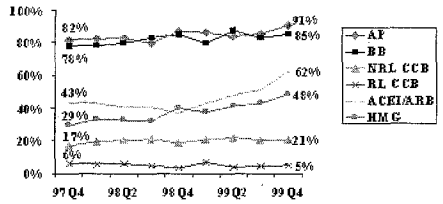
1282 Trends in Acute Myocardial Infarction Management

Wednesday, March 21, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 10:00 a.m.-11:00 a.m.

1282-75 Improving Trends in Evidence-Based Treatment of Acute Myocardial Infarction: Impact of a Population-Wide Disease Management Program?

Jafna L. Cox, Iqbal R. Bata, Blair J. O'Neill, David E. Johnstone, on behalf of the ICONS Investigators. *Dalhousie University, Halifax, NS, Canada*

Background: Despite a wealth of evidence with which to direct clinical practice in cardiology, a care gap persists between actual and ideal rates of use of various treatments. One way of addressing this gap is through disease management, an attractive but hitherto untested paradigm, at least at a population level.
Methods: Improving Cardiovascular Outcomes in Nova Scotia (ICONS) is a large, population based disease management study, involving multiple stakeholders, and funded through a public-private partnership. It has been operational in the province of Nova Scotia since October 1997 where it has focussed on optimizing the care of, among other conditions, acute myocardial infarction (AMI). Research teams operate at 10 sites across the province and trained abstractors carry out detailed chart audits on every single Nova Scotia resident hospitalized with AMI. Information is electronically relayed to the project office in Halifax where it is analyzed and fed back through multiple media to providers and policy makers across the province. Various interventions aimed at optimizing care run concurrently to the data gathering.
Results: Data are provided concerning temporal trends in the discharge rates of various therapies from the start of the project in October 1997 through to the end of 1999. These include antiplatelet therapy (AP), beta-blockers (BB), ACE inhibitors or AII receptor blockers (ACEI/ARB), statins (HMG), as well as rate limiting and non-rate limiting calcium channel blockers (RL CCB and NRL CCB).



Conclusion: Rates of use of evidence-based therapies, already high at the outset of ICONS, have further increased. Therapies for which little evidence for benefit exists in this setting, such as CCBs, have remained correspondingly low. While difficult to prove, it is likely that ICONS has at least stimulated these changes. The final important link to improved outcomes requires longer follow-up.

1282-76 Impact of Prehospital Care in the Management of Acute Myocardial Infarction

Thomas P. Mathew, Ian B. A. Menown, Loreena M. Hill, Jennifer Adgey. *Royal Victoria Hospital, Belfast, United Kingdom*

Background: Pre-hospital care for patients (pts)with acute myocardial infarction (AMI) may improve outcome by enabling earlier administration of fibrinolytic therapy (FT) and management of complications. We prospectively assessed the impact of pre-hospital care in our routine practice. **Methods:** Consecutive pts with AMI presenting out-of-hospital (OH)to a 24 hour physician-manned mobile coronary care unit were compared with those presenting in-hospital (IH)(in the emergency department or other medical wards). We studied 458 pts over a 21 month period (97-99), 200 of whom presented OH, and 258 of whom presented IH. **Results:** OH and IH pts were comparable with respect to age (mean:SD 63.2±12.1 vs 65.1±12.8 years), history of hypertension (62/200:31% vs 73/258:28%), dyslipidemia (149/200: 75% vs 190/258: 74%), current smokers (79/200: 40% vs 99/258: 35%), aspirin on admission (76/200: 38% vs 112/258: 42%), sytolic blood pressure less than 80 mm of Hg on admission (12/200: 6% vs 11/258: 4%) and the number of anterior MI's (67/200: 34% vs 81/258: 31%) p=ns. Male sex(148/200: 74% vs 164/258: 64% p=0.02), ST elevation on admission ECG (171/200: 86% vs 188/258: 73% p=0.001), history of documented ischaemic heart disease (IHD ie:MI or revascularisation)(72/200: 36% vs 67/258: 26% p=0.02), and primary ventricular fibrillation (VF)(33/200: 17% vs 16/258: 6% p =0.0001) were more common in OH pts, whereas diabetes was less common in OH pts (20/200: 10% vs 49/258: 19% p=0.008). FT was more commonly used in OH (157/200: 79%) than in IH pts (136/258: 53%) p =0.0001. Median delay from pain to FT was significantly shorter for OH pts(2.2±3.2 vs 4.1±7.5 hours p=0.0001). Death during hospital stay occurred in 52/458 (11%) pts and was more frequent in IH than OH pts (33/258: 13% vs 19/200: 10% p=0.3). For pts who received FT, mortality was again higher in the IH than OH pts(18/136: 13% vs 11/157: 7% p=0.08). **Conclusion:** Use of pre-hospital care enabled earlier administration of FT and showed a trend towards reduction in early mortality, despite higher incidence of anterior MI's, hypotension, primary VF and previous documented IHD in the OH group.

1282-77 The Smoker's Paradox: Angiographic Insights From the TIMI Trials

Sarah R. Kermgard, Michael S. Chen, Sabina A. Murphy, Jessica S. Lim, Colin A. Hynes, Matthew H. C. Otten, Lily L. Luu, Susan J. Marble, Christopher P. Cannon, Eugene Braunwald, C. Michael Gibson. *University of California San Francisco, San Francisco, CA, Brigham and Women's Hospital, Boston, MA*

Background: Previously, it has been demonstrated that smokers have improved clinical outcomes in the setting of acute myocardial infarction (AMI). We hypothesized that improved outcomes might be explained by improved epicardial and microvascular perfusion, as well as favorable baseline demographics. **Methods:** Data were drawn from the TIMI 4, 10A, 10B and TIMI 14 angiographic trials of AMI. **Results:** Univariate analysis showed that smokers had lower mortality rates (2.57% vs. 6.22%, p=0.001) and lower rates of intracranial hemorrhage (ICH) (0.71% vs. 1.51%, p=0.054). However, in a multivariate model correcting for age and infarct artery location, there was no difference among active smokers and non-smokers in the odds of death (O.R.=0.78, p=0.29, C.I. 0.49-1.24) or ICH (O.R.=0.78, p=0.56, C.I. 0.33-1.81). Higher rates of TIMI grade 3 flow in smokers were confined to those patients with LAD infarctions (TFG 3, 55.7% vs. 43.9%, p=0.006), but no difference was seen in patients with non- LAD infarctions (TFG 3, 64.2% vs. 64.3%). **Conclusion:** Smokers have improved clinical outcomes in AMI. However, this is largely explained by their younger age and lower incidence of anterior AMIs. Despite improved epicardial flow, microvascular flow was impaired (lower TMPG 3 and longer chest pain duration), with larger infarct sizes by peak CK.

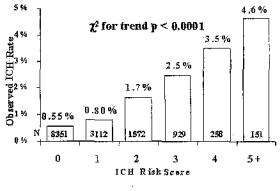
	Smokers	Non-Smokers	p-value
Age	54.4 +/-10.2, n=1240	62.4 +/-10.3, n=1310	<0.0001
LAD Infarct Location	34.5% (425/1232)	39.2% (508/1295)	2 way, 0.01
No. of patients with triple vessel stenosis	16.5% (202/1227)	21.5% (277/1288)	0.001
CTFC (frames)-open and closed arteries	47.9+/-32.9, n=1124	50.8+/-32.7, n=1173	0.002
TIMI Grade 3 Flow	61.2% (722/1179)	56.2% (698/1242)	2 way, 0.01
TIMI Myocardial Perfusion Grade 3	24.3% (91/374)	28.8% (114/396)	2 way, 0.16

Peak CK (CK/upper limit of normal)	13.4+/-13.3, n=1160	11.2+/-10.9, n=1218	<0.0001
Duration of Chest Pain	2.21+/-4.6, n=596	1.7+/-3.6, n=643	0.03

1282-78 Prediction of Intracranial Hemorrhage in the InTIME-II Trial

Michael A. Sloan, Robert P. Giugliano, Susan L. Thompson, Elliott M. Antman, Carolyn H. McCabe, Eugene Braunwald. *Rush Medical College, Chicago, IL, Brigham and Women's Hospital, Boston, MA*

Background: Risk factors for intracranial hemorrhage (ICH) have been established in large coronary thrombolysis trials and registries. Limited data exist on the ability to stratify risk of ICH from thrombolytic therapy.
Methods: In InTIME-II, 15060 patients presenting with ST elevation acute MI at 853 hospitals in 35 countries were randomized in a 2:1 ratio to receive either single-bolus lanoteplase (nPA) 120KU/Kg or 100mg alteplase (tPA) as a 90 minute accelerated infusion. We reviewed the occurrence of ICH in each group, identified independent predictors of ICH in a logistic regression model, and developed a risk stratification scale to identify patients at low and high risk of ICH from thrombolytic therapy.
Results: ICH occurred in 144/15060 (0.96%) of patients enrolled, with 112/10038 (1.12%) in nPA-treated patients, and 32/4990 (0.64%) in tPA-treated patients (p=0.004). Independent predictors of ICH were age ≥75 years (RR=2.77, p<0.0001), prior cerebrovascular disease (CVD) (RR=4.01, p=0.0004), nPA treatment (RR=1.81, p=0.004), weight <67 kg (RR=1.66, p=0.008), prior nifedipine treatment (RR=2.02, p=0.012), SBP >160 mm Hg (RR=1.54, p=0.047), and prior anti-platelet therapy other than aspirin (RR=2.84, p=0.048)(model c-statistic = 0.65). A weighted risk stratification score, after omitting thrombolytic assignment, assigned 4 points for prior CVD; 2 points each for age ≥ 75, prior anti-platelet therapy, prior nifedipine; 1 point each for weight < 67 kg, SBP > 160. ICH rates ranged from 0.55% to 4.6% across 6 risk groups (see figure). Similar patterns of ICH rates were observed across risk groups in separate analyses stratified by thrombolytic agent.
Conclusion: A simple weighted score based on 6 variables can stratify the risk of ICH among patients receiving thrombolysis. This type of risk assessment would be valuable to aid clinicians in the decision to administer thrombolytic therapy.



1282-101 Characteristics and Outcomes in AMI Patients Who Subsequently Develop ST Segment Elevation After Hospital Arrival

Katherine A. Littrell, Mary Lou Skovron, Robert J. Zalenski, Hal V. Barron. *Genentech, Inc., South San Francisco, CA*

Background: The initial ECG is diagnostic of acute injury in approximately 40% of AMIs. The characteristics of AMI patients who develop ST segment elevation (STE) after an initially non-diagnostic ECG and the risk of in-hospital mortality is unclear. OBJECTIVE: The purpose of the study was to determine whether patients who arrive without STE but develop it on a subsequent ECG (STE -/+) are at increased risk of mortality compared to patients who arrive at the hospital with no STE and do not evolve subsequent ST segment elevation (STE -/-). **Methods and Results:** The population consisted of 61,522 AMI patients with an initially non-diagnostic ECG discharged from 1511 U.S. hospitals participating in the NRMI 3 from July 1998 - March 31, 2000. To estimate the increase in mortality risk in patients evolving STE -/+ we used a stepwise multivariate logistic regression model controlling for demographics, presentation characteristics, medications within 24 hours of admission and use of reperfusion strategies. Median time from first 12-lead ECG to 12-lead ECG with STE was a median of 63 min. STE -/+ patients were younger (mean 64.6 vs. 70.6 yrs) and a higher proportion male (67.4% vs. 57.9%) compared with STE -/-. STE -/+ patients less frequently presented with a history of diabetes, previous MI, HTN, CHF, and previous CABG compared with STE -/-. STE -/+ patients were more likely to have chest pain, be a current smoker and present with Killip Class 1. In-hospital mortality was 8.5% for patients with ST -/+ vs. 7.7% in patients with ST -/-. In the multivariate model STE -/+ was associated with a 77% increased odds of in-hospital death compared to STE -/- patients (OR=1.77; 95% CI 1.556-2.013). **Conclusions:** Patients with subsequent STE are younger, more frequently male and have fewer comorbidities compared to STE -/- yet they have a higher risk of in-hospital mortality. The time from initial ECG to subsequent STE suggests that patients evolve STE early in the course of their admission. To optimize diagnosis and management of these patients with STE -/+, a routine practice of early serial ECGs or continuous ST segment monitoring may be advantageous. Further research is necessary to demonstrate the effectiveness of such a routine practice.

1282-102 Time of In-Hospital Death in Patients With Acute Myocardial Infarction Treated With Primary Angioplasty Compared to Patients Treated With Intravenous Thrombolysis. Results From the Pooled Data of the MITRA and the MIR Registries.

Ralf Zahn, Steffen Schneider, Rudolf Schiele, Anselm K. Gitt, Harm Wienbergen, Claus Bossaller, Martin Gottwik, Jochen Senges. *Heart center, Ludwigshafen, Germany*

Background: The in-hospital time course of death in acute myocardial infarction (AMI) after treatment with primary angioplasty (PA) compared to intravenous thrombolysis (TL) is unknown. **Methods:** We analyzed the pooled data of the Maximal Individual Therapy in Acute Myocardial Infarction (MITRA) Registry and the Myocardial Infarction Registry (MIR). **Results:** Out of 8744 lytic eligible patients (pts) with a pre-hospital delay ó12 hours, 7638 (87.4) pts were treated with TL and 1106 (12.6%) pts with PA. The table shows hospital mortality for different time periods.

time after admission	mortality PA	mortality TL	multivariate OR (95%CI)
48 hours	2.7%	4.9%	0.46 (0.30-0.72)
first week	1.6%	2.3%	0.84 (0.49-1.43)
second week	1.5%	1.5%	1.03 (0.56-1.91)
third week	1.4%	0.9%	1.69 (0.74-3.87)
> third week	1.7%	1.5%	0.97 (0.29-3.31)
all	6.2%	9.6%	0.63 (0.47-0.84)

Conclusions: PA is superior to TL for the treatment of pts with AMI. This advantage is achieved during the first 48 hours after admission and is maintained during the hospital stay.

POSTER SESSION

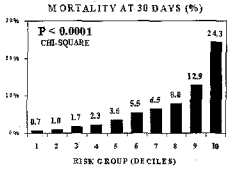
1283 Acute Coronary Syndromes: Clinical and Laboratory Predictors of Outcome

Wednesday, March 21, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 10:00 a.m.-11:00 a.m.

1283-79 Three Simple Factors for Rapid Initial Risk Assessment in ST-Elevation MI: An InTIME II Substudy

David A. Morrow, Elliott M. Antman, Robert P. Giugliano, Richard Cairns, Andrew Charlesworth, Sally S. Cutler, Carolyn H. McCabe, Eugene Braunwald. *Brigham & Women's Hospital, Boston, MA*

Available models for predicting mortality in ST elevation MI (STEMI) include up to 20 clinical factors, but have consistently shown advanced age, increased heart rate and decreased blood pressure to be among the strongest predictors. **Methods:** Using information from multivariable analysis among 14,450 pts with STEMI treated with fibrinolytics in the InTIME II trial, we developed and evaluated a risk index based on age in decades, heart rate (HR) and systolic BP (SBP) for the prediction of mortality by 30 days. The risk index [HR*Decade^2/SBP] was evaluated both as a categorical predictor in deciles, and as a continous variable by logistic regression. **Results:** Age, HR and SBP accounted for 85% of the predictive information available from the full multivariable model. Stratification by the risk index in deciles revealed a highly significant increasing gradient of mortality (Fig). Moreover, the logistic model showed excellent prognostic discrimination (c-statistic = 0.78), comparable to that for the full multivariable model (c-statistic = 0.80). External validation in the TIMI 9 data set (N = 3659) showed a similar strong prognostic capacity (c-statistic = 0.79). **Conclusions:** A very simple risk index using only age, HR and SBP captures the majority of prognostic information offered by a full logistic regression model but is convenient for rapid initial risk assessment in the field or by any clinical provider.



1283-80 Diabetes Doubles the Risk of Death Among Patients Presenting With Acute Coronary Syndromes: Insights From SYMPHONY, a Large International Trial

Darren K. McGuire, L. Kristin Newby, Manju V. Bhapkar, David J. Moliterno, E. Magnus Ohman, F. Chris Dougherty, Robert A. Harrington, Harvey D. White, Frans Van de Werf, Robert M. Califf, Eric J. Topol, the SYMPHONY Investigators. *Duke Clinical Research Institute, Durham, NC*

Background: Diabetes mellitus (DM) is associated with worse outcomes after myocardial infarction (MI). Less is known about the influence of DM, especially on long-term prognosis, following the broader spectrum of acute coronary syndromes (ACS). **Methods:** Baseline characteristics, treatments used, and outcomes were compared between patients with and without DM in the SYMPHONY trial (sibrafiban vs aspirin post-ACS).

Results: 1,577 of 9,233 (17%) patients had DM. DM patients were older, more often female and obese; had more hypertension, hyperlipidemia, and prior cardiovascular disease; and were less often smokers. Patients with DM were more likely to get ACE inhibitors, lipid lowering therapy, calcium blockers and nitrates, and less likely to get ß blockers. There were similar rates of angiography/revascularization in the groups. At 90 days and 1 year (table), DM patients had worse outcomes, including a 2-fold increased risk of death. DM increased the risk of death/MI/severe recurrent ischemia (SRI) at 1 year regardless of the presenting event; (Q Wave MI 18.2% vs 15.6%), non Q Wave MI (25.8% vs 17.5%), or unstable angina (26.6% vs 17.5%).
Conclusion: Diabetes is associated with worse long-term outcomes across the spectrum of ACS. Better treatment strategies are needed for this high-risk population.

Clinical Outcomes by Diabetes Status

Endpoint	DM Patients (%)	Non-DM Patients (%)	OR (95% CI)
90-days			
Death/MI/SRI	12.4	9.5	1.35 (1.14, 1.59)
Death/MI	10.3	6.9	1.55 (1.29, 1.86)
Death	3.4	1.7	2.04 (1.48, 2.83)
1-year			
Death/MI/SRI	23.7	16.8	1.53 (1.37, 1.87)
Death/MI	15.8	10.5	1.60 (1.37, 1.87)
Death	6.0	3.5	1.79 (1.40, 2.27)

1283-81 What Angiographic Measure of Extent of Coronary Artery Disease Best Predicts Subsequent Risk?

David B. Jessup, Joseph B. Muhlestein, Dale G. Renlund, Benjamin D. Horne, Tami L. Bair, Robert R. Pearson, Jeffrey L. Anderson. *University of Utah, Salt Lake City, UT, LDS Hospital, Salt Lake City, UT*

Background: The extent of prevalent coronary artery disease (CAD) is a strong predictor of future risk of cardiovascular events, but the best clinical predictive measure of the extent of CAD is uncertain. We studied the predictive value for death or myocardial infarction (MI) of 6 readily assessed measures of CAD.
Methods: To assess the relationship of CAD measures to outcome, we studied 2827 patients (pt) without acute myocardial infarction (MI) undergoing angiography; 1792 had severe CAD (≥1 stenosis ≥70%), 303 mild/moderate, and 732 no CAD. CAD was quantified in 6 ways: presence of severe CAD, number of vessels with severe disease (≥70% stenosis), moderate/severe disease (>50% stenosis), severe lesions, mild/moderate lesions (10-69% stenosis), and total lesions. Information was entered prospectively into a database, and pt were followed for up to 5.3 years (mean, 2.0 ± 1.4). Associations between measures of CAD and death/nonfatal MI were evaluated using univariate and multivariate Cox regressions (9 co-variables).
Results: Pt were 64 ± 12 years old; 68% were men. During follow-up, 180 pt died and 110 had non-fatal MI. Subsequent death/MI was predicted univariately by all CAD measures (p<.0001), with the order of: number of severe vessels>total lesions>moderate/severe vessels>severe lesions>severe CAD>moderate lesions. In multivariate analyses, all measures retained significance, with the order of: number of severe vessels>severe CAD>moderate/severe vessels>total lesions>severe lesions>moderate lesions. Other independent predictors were ejection fraction, age, diabetes, and hyperlipidemia. Results were generally similar for the endpoint of death alone.
Conclusions: Extent/severity of angiographic CAD was confirmed to be a highly significant and independent predictor of future death/MI. The most powerful single predictor is the number of vessels with severe (≥70%) stenosis. The total number of lesions is a better predictor than number of severe or moderate lesions alone. Simple, qualitative or semi-quantitative measures of angiographic CAD severity provide useful prognostic information.

1283-82 Clinical Implications of the No-Reflow Phenomenon. A Predictor of Left Ventricular Remodeling in Reperfused Acute Myocardial Infarction

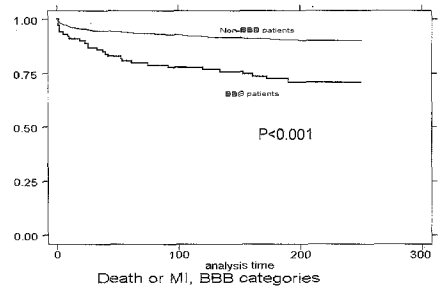
Paolo Colonna, Roberta Montisci, Marco Corda, Christian Cadeddu, Lijun Chen, Enrico Onnis, Luigi Meloni, Sabino Iliceto. *Department of Cardiovascular and Neurological Sciences, University of Cagliari, Cagliari, Italy*

Background: After acute myocardial infarction the damage of microvasculature and the no-reflow phenomenon implies the presence of advanced myocardial necrosis. Intracoronary myocardial contrast echocardiography after acute myocardial infarction can detect the presence and extent of microvascular damage. In this study, we verified the value of early intravenous myocardial contrast echocardiography in predicting left ventricular remodeling after acute myocardial infarction. **Methods:** The study population of 55 consecutive patients with first acute myocardial infarction (20 anterior, 8 lateral and 27 inferior) underwent an echocardiogram on the first day of acute myocardial infarction, a myocardial contrast echocardiography with intravenous injection of Levovist with harmonic power Doppler (Agilent, Sonos 5500) in intermittent imaging mode (triggering 1:3 - 1:5) 2.9±0.6 days after acute myocardial infarction, and an echocardiogram at 3 months follow-up. **Results:** At contrast echocardiography, 37 patients showed contrast enhancement in >50% of acutely dissynergic myocardial segments(reflow) and 18 a sizeable contrast defect (no-reflow). Left ventricular volumes increased in the convalescent stage in patients with myocardial contrast echocardiography no-reflow (end-diastolic from 72.2±15.9 to 101.4±41.8 mL/m2, p<0.0001; end-systolic from 43.3±8.9 to 62.2±35.8 mL/m2, p<0.0001), while remained constant in reflow patients (end-diastolic from 72.1±21.3 to 71.3±16.7 mL/m2, p=ns; end-systolic from 40.1±12.6 to 37.3±13.3 mL/m2, p=ns).
Conclusion: Intravenous myocardial contrast echocardiography with harmonic power Doppler is capable of identifying, in the acute phase of myocardial infarction, patients prone to late left ventricular dilation, thus permitting a more aggressive diagnostic and therapeutic algorithm.

1283-83 Bundle Branch Block Carries a Poor Prognosis for Patients Presenting With Acute Coronary Syndromes. Results From the Prospective Registry of Acute Ischaemic Syndromes in the United Kingdom (PRAIS-UK)

Ameet Bakhai, Marcelo C. Shibata, Julian R. Collinson, Diego Perez de Arenaza, Marcus D. Flather, Jaspal S. Kooner, Jennifer A. A. Adgey. *Royal Brompton and Harefield NHS Trust Hospital, London, United Kingdom*

Background: Patients presenting with MI and bundle branch block (BBB) carry a poor prognosis. The usefulness of BBB as a prognostic marker in patients presenting with non ST elevation acute coronary syndromes (ACS) is not known especially as these patients are usually excluded from most trials.
Method: We enrolled 1,046 patients admitted with non-ST elevation ACS to 56 UK centres (20 consecutive patients per centre) and followed them for 6 months. These centres covered 24% of the UK population and were selected to represent a national cohort.
Results: Baseline characteristics and cardiac outcomes are shown in the table. Death and MI at 6 months occurred in 30% of patients with BBB compared to 11% without BBB, odds ratio=3.52, 95% CI: 2.20 - 5.67 with a multivariate analysis odds ratio of 2.63 (95% CI: 1.60 - 4.32, p<0.001). The outcomes of death or MI at 6 months were higher for patients with LBBB (36%) than those with RBBB (23%) or with ST depression (19%).
Conclusion: Patients with BBB represent 10% of patients with ACS and are older with more risk factors than those without BBB. Despite this, BBB is an independent marker for higher risk of cardiac events than patients with no BBB or even ST depression on the admission ECG. We believe these patients should be treated aggressively on admission with GpIIb/IIIa antagonists irrespective of the results of cardiac markers and coronary interventions considered early.



Death or MI, BBB categories

Characteristics %	LBBB N=57	RBBB N=44	All BBB N=101	Non BBB N=945	P (All vs. Non)
Mean Age (SD)	72 (10)	72 (12)	72 (11)	65 (12)	<0.001
Female	36.8	34.1	35.6	39.7	0.43
Prior MI	64.9	47.7	57.4	47.2	0.05
Diabetes	26.3	22.7	24.7	15.3	0.015
Hypertension	49.1	34.1	42.6	36.5	0.23
MI on admission	12.3	18.2	14.9	14.4	0.90
Outcomes					
Death / MI 7days	8.9	6.8	8.0	4.1	0.07
Death / MI 6mths	35.7	22.7	29.7	10.8	<0.001

POSTER SESSION

1284 Myocardial Ischemia: Left Ventricular Structure and Function

Wednesday, March 21, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 10:00 a.m.-11:00 a.m.

1284-84 Gender-Based Differences in Left Ventricular Structure, Remodeling, and Function After Myocardial Infarction

Franco Macor, Rita Piazza, Pierluigi Temporelli, Eugenio Cervesato, Pantaleo Giannuzzi, Ioanna Stoian, Aldo P. Maggioni, Gianluigi Nicolosi. *Centro Studi ANMCO, Firenze, Italy, Cardiology Dpt A.R.C., Pordenone, Italy*

Background: Despite women affected by myocardial infarction are known to be a subgroup with greater comorbidity and at worse prognosis, their left ventricular (LV) structure, function and remodeling over time have received little attention.

Methods: 757 patients (622 males and 135 females) from the GISSI-3 echo substudy with their first myocardial infarction were considered. Serial echocardiograms were performed 24-48 hours after myocardial infarction (t1), before discharge (t2), after 6 weeks (t3) and after 6 months (t4). Early (t2-t1) and late (t4-t2) LV remodeling was calculated by repeated measures ANOVA.
Results: When compared to men, women were older (70±8 vs 58±12 years, p<0.001), had higher prevalence of hypertension and diabetes (respectively 54 vs 32% and 25 vs 11%, p<0.001) and had larger LV wall motion asynergy (29±15 vs 25±14%, p<0.01). At t1 women had lower LV indexed volumes (diastolic: 71±18 vs 80±19 ml/m^2, p<0.001, systolic: 38±14 vs 42±14 ml/m^2, p<0.005), greater LV diastolic sphericity index (0.44±0.11 vs 0.41±0.09, p<0.005), lower LV ejection fraction (46±8 vs 48±7%, p<0.05), higher prevalence of moderate to severe mitral regurgitation (10 vs 3%, p<0.001), higher LV wall thickness to radius ratio (0.38±0.07 vs 0.35±0.06, p<0.0001) and higher Doppler-derived peak A wave velocity (74±22 vs 66±22 cm/s, p<0.005). After correction for age, LV indexed volumes, diastolic sphericity index and wall thickness to radius ratio remained significantly different between two sexes. Both early and late LV remodeling occurred in women but it did not differ from that of men (time*sex interaction: p>0.10 for diastolic and systolic volumes and sphericity indexes).
Conclusions: Myocardial infarction in women is associated with larger LV damage, more depressed LV systolic function and greater relative LV mass and sphericity. Some of these changes are not due to age differences and their possible prognostic role needs to be further explored. The pattern of early and late LV remodeling did not differ between sexes.

1284-85 Beneficial Effects of Probucol on Neurohumoral Activation and Cardiac Cytokine Expression in the Postinfarction Rat model

Ying T. Sia, Jean-François Sarrazin, Jean-François Jasmin, Angelino Calderone, Jean-Lucien Rouleau. *Montreal Heart Institute, Montreal, PQ, Canada, Toronto General Hospital, Toronto, ON, Canada*

Increased oxidative stress in heart failure may represent an underlying mechanism contributing to the progression of the disease. Indeed, Singal et al. have found that the occurrence of oxidative stress coincides with the appearance of hemodynamic abnormalities secondary to myocardial infarction (MI) in rat. The following study tested the hypothesis that treatment with the antioxidant probucol (PROB) may improve left ventricular (LV) function and morphology in the post-infarction rat and this is associated with inhibition of myocardial cytokine expression and plasma norepinephrine (PNE) secretion. Acute MI was induced by LAD ligation, and at the 20th post-MI day surviving rats were randomized either to placebo or to probucol (61mg/Kg) for 80 days by daily gavage. PROB treatment of sham rats had no effects on either LV function or morpholgy but significantly reduced cardiac TGFb1 and TNFa expression. In the MI group, mean infarct size was 50±2%. As compared to sham rats, MI leads to decreased LV systolic pressure (90±3 vs 131±4mmHg, P<0.05) and +dP/dt (3103±171 vs 6211±370mmHg/s, P<0.05) and increased LV end-systolic pressure (28±2 vs 8±1mmHg, P<0.05). This is accompanied by the increase in LV circumference (35±1 vs 25±3mm, P<0.05), in PNE (938±203 vs 307±77pg/mL, P<0.05) and by a decrease in TNFa expression (0.79±0.02 vs 1.0±0.03pg/mg of tissue, P<0.05) as compared to the sham group. Probucol treatment of MI rats results to improved LV systolic (110±4 vs 90±3mmHg, P<0.05) and end-diastolic pressure (24±2 vs 28±2mmHg, P<0.05)and LV +dP/dt (4250±290 vs 3103±171mmHg/s, P<0.05) as compared to control MI rat. Moreover, LV circumference is reduced in MI rats by probucol (30±1 vs 35±1mm, P<0.05). Likewise, PNE (450±77 vs 938±203pg/mL, P<0.05) and cardiac TNFa (0.67±0.03 vs 0.79±0.02pg/mg of tissue, P<0.05) and TFGb1 (0.13±0.02 vs 1.02±0.13pg/mg of tissue, P<0.05) expression are also inhibited in MI rats by probucol. Theses data indicate that long-term treatment with the antioxidant probucol can improve LV function and morphology in the chronic post-infarction rat model and that part of the underlying mechanism may be the inhibition of cardiac cytokines expression and neurohumoral activation.

1284-86 Biphasic Vascular Structural Response After Myocardial Infarction: A Novel Paradigm for Vessel Remodeling?

Peter Whittaker. *Heart Institute, Good Samaritan Hospital, Los Angeles, CA, University of Southern California, Los Angeles, CA*

Background: A crucial determinant of many vascular injury pathologies is vessel remodeling, which involves both constrictive and expansive forces. The hypothesis to be tested was that injury caused by coronary artery occlusion would result in remodeling of intramyocardial vessels within the infarct.
Methods: The nature and temporal profile of the remodeling was assessed in histology sections of rat hearts examined 1 week (n=8), 3 weeks (n=8), and >3 weeks (n=18, 25±3 weeks) after transmural myocardial infarction (MI). Vessels from uninfarcted hearts (n=14) were also examined. The area ($mm^2 \times 10^{-2}$) occupied by the lumen and muscle was measured by planimetry in 226 vessels.
Results: The muscle:lumen (M:L) ratio increased after MI (*P<0.05 versus control); however, the mechanism for the increase differed over time. At 1 and 3 weeks, lumen area decreased versus control

	Control	1 week	3 weeks	> 3 weeks
M:L ratio	1.54 ± .15	4.06 ±1.04*	4.60 ±1.08*	4.99 ±.84*
Total area	.62 ± .07	.27 ± .05	.36 ± .06	.97 ± .09‡
Lumen area	.26 ± .04	.06 ± .01†	.10 ± .01†	.21 ± .03
Muscle area	.36 ± .04	.21 ± .04	.26 ± .03	.76 ± .08‡

(†P<0.01), but muscle area did not change - consistent with constriction. However, at >3 weeks, lumen area returned to control values, but with an increase in muscle and total vessel area (‡P<0.01 versus all groups), consistent with vascular expansion and muscle proliferation (an increase in nuclei was also seen). These changes were present in vessels that existed prior to infarction and in those that grew afterwards, and were often associated with formation of eccentric lumens.
Conclusions: Intramyocardial vessels undergo biphasic remodeling after MI. The processes of constriction and expansion are similar to restenosis seen after angioplasty and in atheromatous arteries. Thus, the MI model may provide a novel setting for analysis of vascular remodeling, with the advantage that a single experiment produces a large numbers of vessels.

1284-87 Elevated Body Temperature During Acute Myocardial Ischemia Exacerbates Necrosis

Sharon L. Hale, Robert A. Kloner. *Heart Institute, Good Samaritan Hospital, Los Angeles*

In most patients, fever accompanies acute myocardial infarction, beginning within a few hours after the ischemic event, and it often goes untreated. We tested the role of elevated body temperature on infarct size in an open-chest, anesthetized rabbit model of ischemia/reperfusion. **Methods:** Before coronary artery occlusion, body temperature was raised using a heating pad from baseline at 101.4 ± 0.2° F, which is normal in this model, to 104.6 ± 0.3° F in 9 treated rabbits. Temperature in 8 control rabbits was 101.1 ± 0.3° F. Temperature was elevated in treated animals throughout the study. Both groups received 30 min of coronary artery occlusion and 3 hr reperfusion. **Results:** In control rabbits, 36 ± 6% of the ischemic risk region became necrotic, but in hyperthermic rabbits myocardial necrosis was significantly increased to 57 ± 3% of the risk region (p<.005), despite similar risk regions (36 ± 6% of the left ventricle in control and 34 ± 4% in treated hearts, p=ns), and an equal degree of regional myocardial blood flow (RMBF) reduction during ischemia in both groups. Infarct size correlated positively with body temperature (r= 0.66, p<.004). Elevated temperatures caused higher heart rates in hyperthermic rabbits during occlusion (192 ± 6 bpm vs 173 ± 7, p<.01); mean arterial blood pressures were similar in both groups. RMBF was 43% lower during reperfusion in the previously ischemic areas of hyperthermic hearts compared with control hearts (p<.04), suggesting worsened no-reflow. **Conclusion:** Elevation in body temperature by even a few degrees can aggravate necrosis during acute myocardial infarction and may worsen no-reflow. Thus fever might not be just an innocuous side effect of myocardial infarction but should perhaps be treated proactively.

1284-88 Reduction of Ischemia-Reperfusion Injury in the Rat In Vivo by DF1681A, an Inhibitor of Interleukin-8

Laura Calvillo, Riccardo Bertini, Stefano Porzio, Stefano Chimenti, Serge Masson, Francesco Colotta, Roberto Latini. *Istituto di Ricerche Farmacologiche Mario Negri, Milan, Italy, Dompe' Research Center, L'Aquila, Italy*

Background: Leukocytes (PMN) infiltrate the myocardium subjected to ischemia (I) and reperfusion (R), and contribute to the so called R injury. Interleukin-8 (IL-8) is a mediator of PMN migration relevant in IR: a non-protein inhibitor of IL-8 (DF1681A) could reduce R injury. **Methods:** Ischemia was induced in rats by ligation of left coronary artery (I, 30 min) followed by a 4 or 24 h of R. DF1681A was given iv (10 mg/kg bolus) 5 min before R, then sc (8 mg/kg) every 90 min: a dose regimen yielding plasma concentrations found to inhibit PMN chemotaxis in vitro. Before sacrifice, Evans blue was injected to outline non-perfused area (area at risk, AAR). Myeloperoxidase (MPO) and creatine kinase (CK) were assayed biochemically in the AAR. Vehicle treated IR rats (controls) and sham-operated rats were done. Cyclophosphamide (CP) pretreated rats with more than 90' depletion of circulating PMN underwent IR to quantify damage attributable to PMN after 4 h (No=10 for all groups). **Results:** AAR was not different among IR groups (mean 59% of LV mass). After 4 h R, in controls MPO increased by 3.2 folds (p<0.001), and CK decreased by 39% (p<0.01) vs sham-operated. DF1681A reduced MPO increase and CK loss by 77% (p<0.05) and 56% (p<0.05), respectively. In PMN depleted rats, MPO did not increase vs sham-operated, and CK decreased by 14% (p=NS). After 24 h R, in controls MPO increased by 32 folds (p<0.001), and CK decreased by 60% (p<0.001) vs sham. DF1681A reduced MPO increase and CK loss by 46% (p<0.05) and 16% (p<0.05), respectively. **Conclusions:** IR caused infiltration of PMN (MPO increase) and cardiac damage (CK loss) in the AAR which were more marked after 24 h than after 4 h of R. The role of PMN in causing myocardial damage was confirmed by its prevention after PMN depletion with CP. The non-protein IL-8 inhibitor DF1681A, started right before reperfusion reduced PMN migration and CK loss in the AAR. Protection appears to be lower, but still significant, after 24 h of R than after 4 h.

1284-89 Heme Oxygenase-1 Expression and Apoptosis Colocalize in a Rat Myocardial Infarction Model

Päivi Lakkisto, Eeva Palojoki, Antti Saraste, Tom Bäcklund, Liisa-Maria Voipio-Pulkki, Ilkka Tikkanen, Kari Pulkki. *University of Turku, Turku, Finland, Helsinki University Hospital, Helsinki, Finland*

Background: Apoptosis of cardiomyocytes may play a role in the post infarction remodelling. Since there is evidence that induction of heme oxygenase-1 (HO-1) may protect against cell death and apoptosis, we examined the expression and localization of HO-1 in a rat myocardial infarction model. **Methods:** Male Wistar rats were subjected to left anterior coronary artery ligation or sham operation and sacrificed on days 1, 7 and 28. Sections of infarcted hearts were divided into the peri-infarct border area and the non-infarcted remote area. The expression of HO-1 mRNA was assessed by real-time quantitative RT-PCR and the expression of HO-1 protein by immunoconfocal microscopy. **Results:** At 24 hours after ligation HO-1 mRNA was increased about 4-fold in the border vs. remote area or sham operated hearts (p<0.05). At 7 days, HO-1 mRNA levels remained high in the border area. In addition, HO-1 mRNA had increased 2-fold in the remote non-infarcted myocardium (p<0.05). HO-1 mRNA returned to basal levels by 28 days. The increase in HO-1 mRNA was accompanied by increased HO-1 immunoreactivity which was localized into the cardiomyocytes and fibroblasts of the infarct border zone

and vascular structures. According to our previous studies the distribution and frequency of cardiomyocyte apoptosis follows a similar pattern as HO-1 expression. **Conclusion:** HO-1 is induced in a rat myocardial infarction model and the expression of HO-1 colocalizes with apoptosis, suggesting that HO-1 may play a role in the regulation of apoptotic cardiomyocyte loss and ventricular remodelling.

1284-90 Coronary Sinus Oxygen Saturation (SVO2) as a Marker of Myocardial Ischemia

Yves Gallais, Stéphane Champagne, Jin Bo Su, Lucien Sambin, Bertrand Crozatier, Luc Hittinger. *Inserm U400, Creteil, France, Anesthesiology Department, J Rostand Hospital, Ivry /Seine, France*

Background: Coronary sinus oxygen saturation (SVO2) reflects the balance between myocardial oxygen supply and demand. This study was designed to examine whether SVO2 is affected by changes in myocardial blood supply and myocardial contractile function and whether the temporal changes in SVO2 during ischemia are related to temporal ECG ST segment changes. **Methods:** Eight open-chest dogs were instrumented with a left ventricular pressure gauge, an oxymetry Swan-Ganz catheter in the coronary sinus for continuous SVO2 monitoring, a circumflex coronary cuff occluder, a doppler flow probe to measure circumflex coronary blood flow velocity (CBFv) and piezo-electric crystals to measure left ventricular anterior and posterior wall thicknesses. Myocardial blood supply and myocardial contractile function were modified by partial coronary stenosis (50% reduction in CBFv, 3min), total coronary occlusion (zero CBFv, 3min), ATP injection (20 mg iv) and dobutamine infusion (10 µg/kg/min, iv). **Results:** SVO2 changes were closely correlated to CBFv changes induced by coronary stenosis, coronary occlusion and ATP injection ($r=0.784$, $p<0.001$) and also to left ventricular posterior wall thickening changes induced by coronary stenosis, coronary occlusion and dobutamine infusion ($r=0.851$, $p<0.001$). SVO2 was reduced ($p<0.001$) 15 seconds after the onset of coronary occlusion from 38±1% to 12±2% while ECG ST segment changes reached the significant threshold (1 mv) 60 seconds after coronary occlusion. During partial coronary stenosis, SVO2 was reduced from 38±1% to 26±2% ($p<0.01$) 75 s after the onset of partial coronary stenosis while ECG ST segment changes never reach the significant threshold during the 180 s period of coronary stenosis. **Conclusion:** SVO2 reduction is associated with myocardial ischemia. SVO2 measurement is a more sensitive marker of myocardial ischemia than ECG ST segment analysis and may be useful in the monitoring of myocardial ischemic events during cardiac or non cardiac surgery.

POSTER SESSION

1285 Stabile Ischemic Syndrome: Pathophysiology, Diagnosis, and Prognosis III

Wednesday, March 21, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 10:00 a.m.-11:00 a.m.

1285-91 RSR` Pattern Without the Evidence of Bundle Branch Block: Diagnostic Value as a Sign of Left Ventricular Aneurysm

Mithilesh K. Das, Kuruvilla Cheriparambil, Majesh Makan, John Kassotis, Barry Saul, Chatla C. V. R. Reddy. *Cornell University Medical College, New York, New York Methodist Hospital, Brooklyn, NY*

Background: A left ventricular aneurysm (LVA) is associated with increased risk of heart failure, thromboembolism, ventricular arrhythmias and also the increased risk of sudden and non-sudden death. An RSR` pattern without evidence of bundle branch block ( QRS duration ≤120ms) on the ECG may be associated with a LVA as a result of myocardial scar formation . A LVA is common in the anterolateral and circumapical region of the left ventricular wall. We, therefore, postulate that an RSR` pattern in the left sided leads (I, aVL,V3 to V3) is a highly specific sign of LVA. **Methods:** ECG's of 110 consecutive patients with LVA documented by left ventricular angiography (30o right anterior oblique view) was compared with 110 patients without LVA. **Results:** The RSR` pattern or its variant (RSr`, rSR` or RsR`) pattern on left sided leads were present in 55(50%) patients with LVA as compared to 6 (5%) patients without LVA (p value <0.0005). The sensitivity of RSR` pattern for LVA was only 50% whereas the specificity was 94.5%. The false negative and the false positive rates were 50% and 5.4%, respectively. It has a high positive predictive value of 90% with a relatively moderate negative predictive value of 65%. The overall accuracy of the test is 75%.

Total no. of patients studied	Patients with LAA (N= 110)	Patients without LAA (N = 110)
Positive results (RSR` present)	63 (True Positive)	6 (False positive)
Negative results(RSR` absent)	47 (False negative)	104 (True negative)

Conclusion: Our study has revealed that an RSR` pattern in the left sided leads, as a highly specific and moderately sensitivity sign of LVA. It also has high positive predictive value.

1285-92 Who Refers Negative Coronary Angiograms?

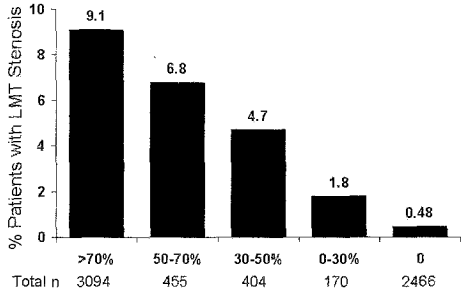
Dominic Y. Leung, Craig P. Juergens, Sidney Lo, Andrew P. Hopkins. *Liverpool Hospital, Sydney, Australia*

Background: Coronary angiography is the definitive test for suspected coronary disease. However, the referral patterns and referrer characteristics of angiographically normal coronary arteries or minor disease (negative angiogram) in patients with suspected coronary disease are seldom reported.
Methods: From 12/92 to 7/00, a total of 6,409 patients underwent 8,069 coronary angiograms at Liverpool Hospital. Only studies referred primarily for coronary disease (n=6,862) were analyzed. Studies for valvular disease (n=279), failed access (n=52) and angioplasty (n=876) were excluded. Patient characteristics, main practice location and specialty of referrers were correlated with the negative angiogram rate.
Results: 783 patients (790 procedures, 12.5%) had normal coronary arteries. 719 patients (740 procedures, 11.7%) had minor disease (<50% stenosis on >=1 epicardial coronary artery). For referrers with >40 referrals (n=33, mean referrals 191±244, range 42 - 1102), negative angiogram rate was 22±8% (10 - 41%). Cardiologist referrers (n=20) had a higher negative rate compared with non-cardiologist (n=13) referrers (25±7% vs 18±6%, p=0.005). Proceduralists (n=9) had similar negative rate compared with non-proceduralists (n=24, 24±4% vs 21±9%, p=NS). Referrers with main practice in Liverpool area had a higher negative rate compared with referrers outside Liverpool area (25±8% vs 19±5%, p=0.019). There was no difference in the negative rate before and after coronary surgery and angioplasty services commenced at Liverpool Hospital (8/97, 24.7% vs 24%, p=NS). Multiple logistic regression revealed patient aged <=50 years (OR 2.8), female gender (OR 2.9), cardiologist referrer (OR 1.5) and referrer with closer access to catheterization laboratory (OR 1.2) to be significant independent predictors of negative angiogram.
Conclusions: Negative angiogram rate varied widely between referrers. Cardiologists had a higher negative rate compared with non-cardiologist referrers. Whether the referrer was a proceduralist did not affect the negative rate. The availability of revascularization service did not but the easier access to a catheterisation laboratory did affect the negative rate.

1285-93 Isolated Left Main Trunk Stenosis: How Common Is It?

Samir R. Kapadia, Gary V. Martin, J. Ruben Flores, Richard V. Anderson, James H. Caldwell, Kenneth G. Lehmann. *VA Puget Sound Health Care System, Seattle, WA, University of Washington, Seattle, WA*

Background: Identification of left main (LMT) stenosis in the cardiac catheterization laboratory is critically important not only for patient management but also to increase safety of the catheterization procedure. Occasionally LMT stenosis is not associated with significant atherosclerosis of other epicardial coronary vessels. We sought to determine the prevalence of isolated left main stenosis from a prospective registry of consecutive patients. **Methods:** At our institution 8004 patients underwent diagnostic cardiac catheterization between 1990 and 2000. Patients with prior by-pass surgery (n=1415) were excluded from the analysis, as the natural history of LMT stenosis in these patients may be different. Prevalence of LMT stenosis (>=50%) was studied according to the severity of the most severe lesion in the coronary arteries other than the LMT. The patients were divided into 5 groups. Group 1 included patients with the most severe lesion >70%, group 2 between 50-70%, group 3 between 30-50%, group 4 between 0-30% and group 5 with patients having no angiographically identifiable lesions. **Results:** Significant LMT stenosis was detected in 348 (5%) patients. Significant lesions (>70%) in other coronary arteries were more frequently present in patients with LMT stenosis than in patients without (81% vs 45%). The prevalence of LMT stenosis in association with presence of other coronary artery lesions is shown in the figure. Significant LMT stenosis was almost 20 times less likely to be present in patients with otherwise normal coronaries compared to patients with other significant coronary lesions.(0.48% vs 9.1%) **Conclusion:** Isolated LMT stenosis is rare. Therefore, when encountered in the cath lab, careful angiographic determination supplemented with appropriate use of intravascular ultrasound is warranted to help exclude misleading angiographic views or catheter induced spasm.



1285-94 Differences in Presentation and 1 Year Outcomes in Coronary Artery Disease (CAD) Patients of South Asian vs European Ethnicity Treated in an Outpatient Cardiology Practice

Narendra Singh, Milan K. Gupta, Arsh k. Jain, Frank Halperin, David Borts. *Rouge Valley Health System, Toronto, ON, Canada, William Osler Health Centre, Brampton, ON, Canada*

Background: Previous studies have shown differences in cardiac presentation and worse outcomes for South Asian (SA) vs European Canadian (EC) hospitalized inpatients. **Methods:** We retrospectively reviewed 400 consecutive outpatients with CAD having 1 yr follow-up with respect to pt ethnicity, cardiac risk factors, utilization of evidence-based drug therapies, hospitalization and outcomes over 1 year (1996-97). **Results:** Of the 400 pts, 65% were males, 22% were SA. Mean age was 60+11 yrs. Comparison of SA vs EC pts showed SA pts were slightly younger (59 vs 61 yrs, p=.09), more often diabetic (37 vs 20%, p=0.001) less often smokers (29 vs 54%, p=.001), and had similar risk factors of hyperlipidemia (44 vs 49%) hypertension (54 vs 49%) or family Hx of CAD (24 vs 34%) p=ns. At initial visit 49% were on ASA, 33% beta-blockers, 20% statins, and 26% ACE inhibitors. SA patients were less likely to be on an ACE inhibitor at presentation 18 vs 28%, p=0.001. Utilization increased substantially to 73%, 45%, 55%, 32% respectively at 1 yr. No significant difference in utilization between SA vs EC pts was noted at 1 year. At 1 yr, SA pts as compared to EC pts, were more likely to have quit smoking (50% vs 9%,p=.001) but had poorer BP control (142/81 vs 137/78 mmHg, p=.01), similar fasting glucose levels (6.5 vs 7.3 mmol, p=ns), similar LDL (3.0 vs 2.8mmol,p=ns) but lower HDL (1.06 vs 1.17mmol,p=0.02) levels. Cardiac hospitalizations (36% vs 41%) and revascularization (17 vs 20%) occurred frequently after initial consultation but were no different between the groups at 1 yr. **Conclusions:** SA outpatients have a different CAD risk factor profile than EC patients both at presentation and at 1 yr follow-up. Utilization of evidence based drug therapies at 1 yr improved following cardiology consultation and may explain the similar outcomes despite differences at presentation. These data suggest that early intervention by cardiologists for this high risk ethnic population could potentially reduce subsequent morbidity and mortality.

POSTER SESSION

1286 Defining Modalities of the Acute Coronary Syndromes

Wednesday, March 21, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 10:00 a.m.-11:00 a.m.

1286-95 Atypical Presentations Among Medicare Beneficiaries With Unstable Angina: Is It Time to Redefine the Classical Clinical Presentation?

John G. Canto, Contessa Fincher, Catarina I. Kiefe, Jeroan J. Allison, Qing Li, Suzanne Baker, Robert Centor, Norm W. Weissman. *University of Alabama at Birmingham, Birmingham, AL*

Background. The presence of chest pain (CP) is a hallmark symptom in patients with unstable angina (UA). However, little is known regarding the prevalence of atypical presentation among these patients and their related symptoms. **Methods.** We examined the medical records of 3,015 Medicare patients hospitalized at 22 Alabama hospitals with a confirmed diagnosis of UA between 1994 and 1998. Confirmation of UA required that the presenting symptom(s) be consistent with an acute coronary syndrome by documentation of the admitting physician, and that there be no evidence of acute myocardial infarction at the time of initial presentation. We categorized the presenting characteristics into typical or atypical. Typical presentation was defined as 1) CP located substernally, in the left chest, or right chest; and 2) the character of CP described as squeezing, tightness, aching, crushing, discomfort, dullness, fullness, heaviness, pressure, relieved with rest or nitroglycerin, or worse with activity. Atypical presentation was defined as the absence of 1), 2), or both.

Results

Table 1. Comparison of Atypical and Typical Patients

	Atypical Presentation	Typical Presentation	P Value
N (%)	1,342 (44.5)	1,673 (55.5)	
Mean age, years	73.0	71.0	< 0.001
Women, %	58.3	54.6	0.05
Non-White, %	43.2	56.8	0.61
Diabetes, %	43.7	56.3	0.55
Hypertension, %	44.7	55.3	0.77
Prior MI, %	41.8	58.2	0.02
Mortality - hospital, %, (N=18)	50.0	50.0	0.73
Mortality - 30 days, %, (N=358)	47.2	52.3	0.27
Mortality - 1 year, %, (N=509)	46.8	53.2	0.26

Table 2. Presentation Characteristics of Atypical Patients

Atypical chest pain, %	5.1
Pain in other region (jaw, shoulder, arm, neck, face, ear, epigastric), %	32.3
Shortness of breath, %	73.9
Nausea, %	40.2
Vomiting, %	10.8
Diaphoresis, %	27.7
Syncope, %	10.7

Conclusion. Almost one-half of all elderly Medicare patients with confirmed UA had "atypical" presentations. Important characteristics of these patients included age, gender and no prior MI, but not race. Our results suggest that the classical presentation of UA may need to be redefined and that national educational initiatives to increase awareness of atypical presentations in UA are indicated.

1286-96 Site Investigators Do Not Accurately Report Myocardial Infarction Events: Results of Event Adjudication by a Clinical Events Committee in the PARAGON-B Trial

Kenneth W. Mahaffey, Patricia A. Connolly, Matthew T. Roe, Rodney Sparapani, Lisa G. Berdan, Neal S. Kleiman, Debra Fasteson, Christopher B. Dyke, Maria C. Bahit, Darren K. McGuire, Kristin L. Newby, Paul W. Armstrong, Robert M. Califf, Eric J. Topol, Robert A. Harrington. *Duke Clinical Research Instiute, Durham, NC*

Background: Myocardial infarction (MI), an important clinical trial endpoint, can be difficult to classify due to inconclusive symptoms, enzyme data, or electrocardiograms. In prior trials, disagreement between MI events reported by site investigators and a clinical events committee (CEC) have been observed.
Methods: To better understand disagreements in MI reporting between investigators and a CEC, we analyzed data from the PARAGON–B trial which evaluated the glycoprotein IIb/IIIa inhibitor, lamifiban, in 5,225 patients with acute coronary syndromes. The primary endpoint was the 30-day composite of death, MI or recurrent ischemia. All suspected MIs were adjudicated by a CEC.
Results: Overall, 1,736 patients (33%) had suspected MIs identified from data on the case report form; 483 (28%) were adjudicated by the CEC as MIs that met protocol endpoint criteria. In 404 (23%) patients, investigator and CEC assessments of MI differed; 270 MIs were identified by the CEC but not the investigators, and 134 were identified by investigators but not the CEC. To prospectively reconcile disagreements between the CEC and the investigator, we sent letters to investigators that described the disagreement and asked for re-evaluation by the investigator. For the 404 patients with disagreement, letters were sent and returned for 382 patients. The remaining 22 had clear MIs by core lab enzyme criteria. Investigators came to agree with CEC assessments in 307 (80%). For the remaining 75 cases (20%); the CEC supported investigators' assessments in 10 and confirmed original CEC decisions in the other 65 cases. Of cases with persistent disagreement, 44% were periprocedural MIs but 20% were enzyme elevations associated with ischemic symptoms and/or ECG changes.
Conclusions: Investigators underreported MI endpoints, but most agreed with CEC assessments of MIs after further follow-up. We support standardized, independent adjudication of suspected MI endpoints in order to accurately identify MI endpoint events. Disagreements may be due to inadequacies in event ascertainment using standard case report form tools as well as differences in MI definitions used in clinical trials compared with clinical practice.

1286-97 Cost-Effectiveness of Early Invasive Treatment in Unstable Coronary Artery Disease: A One-Year Follow-Up From the FRISC II Invasive Trial

Magnus Janzon, Lars-Åke Levin, Eva Swahn, FRISC II Investigators. *Institution of Medicine and Care, Linköping University, Linköping, Sweden, CMT, Center for Medical Technology Assessment, Linköping University, Linköping, Sweden*

Background: Both early invasive and non-invasive treatment strategies in patients presenting with unstable coronary artery disease have been used during the acute phase of the disease. It has not until recently been conclusively demonstrated which of these strategies has a better clinical outcome. Until today there is no prospective study analysing the economic implication in this important and large patient group in the long-term follow-up. The aim of this study was to evaluate the cost-effectiveness of early invasive strategy.
Methods: We determined in-hospital and one-year follow-up costs for 2 457 patients in the FRISC II trial with unstable angina or non-Q-wave myocardial infarction who were randomised to early invasive or non-invasive treatment. Medical costs as hospitalisations, investigations, interventions, pharmaceuticals and outpatient visits as well as non-medical costs as loss of production and home care were documented prospectively. The costs were based on Swedish hospital charges at 1997 price level. **Results:** In the FRISC II trial the invasive treatment showed a reduction in the incidence of death or MI (10.4 % vs. 14.1 %, p=0.005). In the cost analysis there was a significant higher cost in the invasive group. The cost difference per patient was 27.500 SEK (2.900 US$). The cost-effectiveness ratio was 740.000 SEK (77.000 US$) per avoided event, myocardial infarction or death. Expressed in cost per life saved the cost-effectiveness ratio was 1.6 MSEK (167.000 US$). **Conclusions:** Due to the costly initial interventions there was still a higher total cost in the invasive treatment group at one-year follow-up. The cost-effectiveness ratio was 740.000 SEK (77.000 US$) per avoided myocardial infarction or death. To determine the final cost-effectiveness ratio for invasive strategy a longer follow-up period is needed as well as the use of QALYs, quality adjusted life years.

1286-98 **Relationship Between ST Segment Elevation After Acute Myocardial Infarction and Microvascular Reperfusion Injury Evaluated With Myocardial Contrast Echocardiography**

Paolo Colonna, Abdel Hakeem Seleem, Marco Orrù, Chrisian Cadeddu, Roberta Montisci, Lijun Chen, Enrico Onnis, Luigi Meloni, Sabino Iliceto. *Department of Cardiovascular and Neurological Sciences, University of Cagliari, Cagliari, Italy*

Background. After acute myocardial infarction, the return to baseline of ST segment in the surface electrocardiogram predicts good myocardial functional recovery and prognosis. In patients with acute myocardial infarction the microcirculatory reperfusion may remain impaired due to a process of microvascular injury, detectable with intravenous myocardial contrast echocardiography. We hypothesized that patients with a rapid ST segment return to baseline have a better microvascular preservation at myocardial contrast echocardiography. **Methods.** Seventeen patients with a first anterior acute myocardial infarction, 9 treated with primary PTCA and 8 with intravenous thrombolysis, were studied. A surface ECG was obtained at admission and after recanalization (90 minutes after admission ECG); the ST elevation was summed in all anterior leads and the percentage of recovery of the summation at 90 minutes ECG was computed. Intravenous myocardial contrast echocardiography (Levovist rapid infusion) with harmonic power Doppler (Agilent Sonos 5500) and ECG triggering every 3 to 5 fives cardiac cycles was performed 2.8±0.4 days after the acute phase. The no-reflow extent was computed as the percentage ratio of segments not opacified to the total segments in the risk area. Patients were considered to have no-reflow if its extent was ≥ 50% of the total myocardial segments in the risk area. **Results.** No-reflow phenomenon was present in 6 of the 7 (85.7%) patients with persistent (>50% of initial value) ST segment elevation after recanalization, while only in 2 of the 10 (20%; $p<0.05$) patients with ST segment resolution. The average no-reflow extent at contrast echocardiography was 60.1±22.2% in patients with persistent ST elevation versus 28.8±37% ($p<0.05$) in patients with ST resolution. **Conclusion.** In acute anterior myocardial infarction the persistence of ST segment elevation after recanalization is suggestive of more extensive microvascular damage, as detectable with intravenous myocardial contrast echocardiography.

1286-99 **In Patients With Unstable Angina High Levels of C-Reactive Protein Are Associated With Irregular Plaques in Carotid Arteries: A Sign of a Diffuse, Systemic Inflammatory Involvement?**

Pasquale Silvestri, Luigi M. Biasucci, Giovanna Liuzzo, Attilio Maseri, Antonella Lombardo. *Catholic University, Rome, Italy*

Background: In unstable angina (UA) high levels of inflammatory mediators, such as C-reactive protein (CRP), has been demonstrated in up to 65% of pts. However it is still unknown whether this response is associated with a selective coronary or a more general arterial instability. **Methods:** In order to evaluate whether the inflammatory response is associated with an unstable morphology of atherosclerotic plaques in other vascular districts, we performed Color-Doppler-Echography of carotid arteries in 46 pts admitted to our Coronary Care Unit (CCU) with Brauwald's class IIIB UA. Extracranial carotid arteries were classified as: normal (no plaques); arteries with smooth plaques (smooth surface and homogeneous echogenicity also in the presence of calcifications) and arteries with irregular plaques (irregular surface or dishomogenous echogenicity). On admission to CCU, CRP levels were assessed by high sensitivity nephelometry (Dade-Behring Latex NII) in all pts. **Results:** 15 pts had irregular plaques, 15 pts had smooth plaques and 16 pts had normal carotid arteries. CRP levels were significantly higher in pts with irregular plaques than in those with smooth plaques and with normal carotid arteries (respectively: median: 8.8 mg/L [range 2.5-27.8], 2.1 mg/L [0.8-11.6], 3.35 mg/L [0.7-19.5], $p<0.05$ irregular plaques vs regular and normal arteries). **Conclusions:** Unstable angina patients with irregular carotid artery plaques have CRP levels higher than UA patients with normal carotid or smooth plaques. Thus, our data suggest that in UA a common inflammatory mechanism may be associated with instability of coronary and carotid plaques.

1286-100 **Coronary Artery Calcification in Patients With Acute Chest Pain**

Dimitris Alexopoulos, Christos Stathopoulos, George Hahalis, John A. Chiladakis, Abraham Kotsaridis, Antonis S. Manolis. *Patras University, Patras, Greece*

Background: Coronary artery calcification (CAC) indicates presence of atherosclerotic plaque. Many patients (pts) with acute chest pain due to ischemia or infarction present to the emergency department (ER) with diagnostic difficulties due to non-ischemic electrocardiogram (ECG) and normal cardiac enzymes (CE).The aim of this study was to assess whether CAC is a useful adjunct for risk stratification in pts with acute chest pain. **Methods:** 74 pts (51 men) with no prior history of coronary artery disease (CAD), mean age 57+/-10 years, were admitted to the hospital for evaluation of acute chest pain. Pts had a non-diagnostic ECG and normal CE in the ER. Within 24 hours from admission, all pts underwent digital cinefluoroscopy of the heart in the 45oLAO/15oCRANIAL projection for about 5 sec and the video recording was then examined for the presence of CAC. Pts were divided into 2 groups: Group-A, with CAC (n=30) and Group-B without CAC (n=44). All pts were monitored for 24 hours and serial CE (CPK, CPK MB) and ECGs were obtained at 0, 8, 16 and 24 hours.A negative evaluation led to an exercise stress test (EST). Pts with a negative EST were discharged home, while pts with a positive EST underwent dobutamine stress echo or thallium-201 scintigraphy, and/or coronary angiography. CAD was considered present if a pt had: 1) elevated CE 2) subsequent ECG changes suggestive of infarction or ischemia 3) abnormal dobutamine stress echo or thallium-201 scintigraphy and/or coronary angiography. **Results:** Table

	Group A	Group B	p value		Group A	Group B
Age	60+/-9	55+/-10	0.039	CAD+	23 (77%)	5 (11%)
Men	26(87%)	25(57%)	0.001	CAD-	7 (23%)	39 (89%)
Risk factors for CAD	2.6+/-1	2.0+/-1	0.048		p<0.0001	

(Fisher's exact test, unpaired t-test) (Fisher's exact test)

The presence of CAC had 82% sensitivity, 85% specificity, 77% positive predictive value and 89% negative predictive value for detection of CAD (relative risk = 6.7). Male gender, advanced age and the presence of risk factors for CAD were more frequent in pts with CAC. **Conclusion:** CAC detected by digital cinefluoroscopy can be useful for the management of pts with acute chest pain, presenting to the ER with a non-diagnostic ECG and normal CE.

ORAL CONTRIBUTIONS

889 Limitation of Infarct Size: Novel Approaches

Wednesday, March 21, 2001, 10:30 a.m.-Noon
Orange County Convention Center, Room 230B

10:30 a.m.

889-1 **LXR1035 a Novel Lysophosphatic Acid Analog Attenuates Ischemia-Reperfusion Injury**

Christian Zellner, Richard E. Sievers, Amanda E. M. Browne, Samuil R. Umansky, J. Graham Goddard, William W. Parmley, Kanu Chatterjee, Randall J. Lee. *University of California, San Francisco, San Francisco, CA, LXR Biotechnology Inc., Richmond, CA*

Background: Modulation of apoptosis is a promising pharmacologic target in the treatment of myocardial infarction. We studied the effects of LXR1035, a novel analog of lysophosphatidic acid, on cardiac myocytes in cell culture and on myocardial infarction and ischemia-reperfusion (IR) injury in vivo. **Methods:** Apoptosis was induced in rat neonatal cardiomyocytes using glucose deprivation and hypoxia/normoxia, simulating apoptosis after IR injury. Upregulation of caspase-3 and DNA fragmentation were quantified to assess degree of apoptosis. To test the hypothesis that LXR1035 reduces myocardial IR injury in vivo, rats pretreated with either vehicle (n=10) or LXR1035 (75nmol/kg/h and 750nmol/kg/h, n=8 for each dose) were subjected to 17min of occlusion of the left coronary artery (LCA) and 2 hours of reperfusion. Infarct size and area at risk were determined using triphenyltetrazolium chloride and blue dye staining and digital image analysis. **Results:** In cell culture, LXR1035 prevented all steps in apoptotic cell death including caspase-3 activation, internucleosomal DNA degradation, cell permeabilization and detachment. The effects on cell survival were superior to classic caspase inhibitors, particularly in the setting of simulated IR injury, suggesting that LXR1035 modulates multiple pathways in apopototic cell death. In vivo studies of myocardial IR showed that the percent myocardial infarct per heart was significantly reduced with low and high doses of LXR1035 (22.9±9.4 and 22.4±8.9, respectively for 75 and 750nmol/kg/h) as compared to control (35.3±11.4). Percent infarct for area at risk was also significantly reduced with low and high doses of LXR1035 (37.0±12.2 and 39.2±13.7), respectively for 75 and 750 nmol/kg/h) as compared to control (55.3±10.6). **Conclusions:** Treatment with the structural analog of lysophospatic acid LXR1035 attenuates myocardial IR injury by modulation of multiple pathways of apoptotic cell death. LXR1035 may thus have utility as adjunct therapy in both catheter-based and pharmacologic reperfusion strategies for acute myocardial infarction by preventing IR injury.

10:45 a.m.

889-2 **Blockade of Lectin-Like Oxidized Low-Density Lipoprotein Receptor Reduces Myocardial Infarction Size After Ischemia-Reperfusion**

Kazuaki Kataoka, Ryuji Nohara, Koji Hasegawa, Tetsuhiko Yanazume, Taku Hirai, Tatsuya Sawamura, Masatoshi Fujita, Shigetake Sasayama. *Department of Cardiovascular Medicine, Graduate School of Medicine, Kyoto University, Kyoto, Japan. Department of Bioscience, National Cardiovascular Center Research Institute, Suita, Japan*

Background: Lectin-like oxidized low-density lipoprotein receptor (LOX-1) is a receptor for oxidized low-density lipoprotein. Recent reports indicated that LOX-1 mediates oxidized low-density lipoprotein-induced apoptosis and intracellular production of reactive oxygen species. Since several studies have revealed that apoptosis and reactive oxygen species have significant role in myocardial reperfusion injury, we are interested in examining whether blockade of LOX-1 reduces myocardial infarction size after ischemia-reperfusion. **Methods:** Male Wistar rats, weighing 300 g were used. Polyethylene catheters were placed in the internal carotid artery and the femoral vein for measurement of arterial blood pressure and infusion of drugs. Myocardial ischemia was induced by ligation of the left coronary artery for 1 hour, followed by reperfusion. The anti-LOX-1 monoclonal antibody (Group A; n=7) and normal IgG (Group B; n=7) were administered 15 minutes before and 30 minutes after coronary ligation in a total dose of 5 mg/kg. Control rats were received normal saline (Group C; n=7). Two hours after the reperfusion, the rats were sacrificed to remove the hearts for the determination of the area at risk and infarct size by staining with patent blue violet and triphenyltetrazolium chloride, respectively. **Results:** There were no significant differences in heart rate or mean arterial blood pressure

among the three groups. The percentage of the area at risk did not differ among the three groups (Group A; 37.6±8.7%, Group B; 34.0±8.9%, Group C; 39.2±12.2%). However, Group A (21.2±17.2%) displayed a 50% reduction in myocardial infarct size compared with Group B (42.5±7.4%) or Group C (38.3±11.5%) (P<.05). **Conclusions:** The present study demonstrates that administration of anti-LOX-1 monoclonal antibody significantly reduces myocardial infarction size after ischemia-reperfusion in spite of no differences in hemodynamic data and size of the area at risk. These data suggest that the LOX-1 pathway is involved in the extent of myocardial ischemia-reperfusion injury and that inhibition of LOX-1 is feasible for treatment in acute myocardial infarction.

11:00 a.m.

889-3 **Inhibition of Mannose Binding Lectin Reduces Myocardial Reperfusion Injury: A Role for the Lectin Complement Pathway in Cardiovascular Disease**

James E. Jordan, Gregory L. Stahl. *CET&RI, Dept. of Anesthesia, Brigham and Women's Hospital, Boston, MA*

Background: Complement activation plays an undeniably important role in the pathogenesis of myocardial ischemia-reperfusion injury. However, the initiating mechanism of complement activation in this setting is largely unknown. We have recently demonstrated that the lectin complement pathway is activated by mannose binding lectin attaching to human endothelial cells following oxidative stress, suggesting that inhibition of mannose binding lectin may afford tissue protection following periods of ischemia and reperfusion. **Methods:** In the present study, we developed a monoclonal antibody (mAb P7E4) that functionally inhibits rat mannose binding lectin and evaluated its cardioprotective effects in an established model of myocardial ischemia and reperfusion. Rats (n=7/group) were treated with an isotype control mAb or P7E4 (0.05 or 1 mg/ml) 5 min prior to occlusion of the left anterior descending coronary artery for 30 min. Following 4 hrs of reperfusion, the hearts were excised and evaluated for mannose binding lectin and C3 deposition, infarct size (triphenyl-tetrazolium chloride staining), creatinine kinase activity and neutrophil infiltration (myeloperoxidase). **Results:** Mannose binding lectin and C3 deposition was apparent on the coronary vasculature following myocardial ischemia and reperfusion and was decreased with P7E4 treatment. Pretreatment with P7E4 significantly reduced infarct size (area of necrosis/area at risk) in a dose-dependent manner compared to an isotype control (Isotype control: 62±1% vs 55±1% and 38±1% for 0.05 and 1 mg/kg P7E4, respectively). Left ventricular loss of creatine kinase was significantly reduced by 1mg/kg P7E4 compared to control (2.7±3.4 vs 11.0±2.0 U/mg protein, respectively). Similarly, myocardial myeloperoxidase activity was significantly decreased by P7E4 compared to control (1.1±0.3 vs 2.4±0.2 U/mg protein, respectively). **Conclusion:** These data demonstrate that inhibition of mannose binding lectin, the first molecule of the lectin complement pathway, protects the rat myocardium from ischemia and reperfusion-induced injury.

11:15 a.m.

889-4 **Effects of Different Durations of Pretreatment With Losartan on Myocardial Infarct Size and Endothelial Function**

Bo-Qing Zhu, Yi-Ping Sun, Richard E. Sievers, Amanda E. M. Browne, Randall J. Lee, Kanu Chatterjee, William W. Parmley. *University of California San Francisco, San Francisco, CA*

Background: Our previous studies showed that 10 weeks of pretreatment with the AT1 receptor antagonist losartan reduced myocardial infarct size and arrhythmias in a rat model of ischemia-reperfusion. However, the effect of a differing time course of pretreatment has not been investigated. **Methods:** 104 Sprague-Dawley rats were randomized into 4 groups: a control, and 3 pretreatment groups in which losartan was given 40 mg/kg/day in drinking water for 1 day, 1 week, and 4 weeks respectively. After different durations of pretreatment, the rats were subjected to 17 min of left coronary artery occlusion and 120 min of reperfusion with hemodynamic and ECG monitoring. Effective refractory period (ERP), VF threshold, angiotensin II (Ang II) levels in plasma, and infarct size were measured. Aortic rings were removed for vascular reactivity studies. Vascular endothelial growth factor (VEGF protein) in the ischemic myocardium was measured by Western blot analysis. VEGF change was expressed relative to control (1.0). **Results:** The mortalities during the occlusion and reperfusion period were not different among the four groups. The hemodynamic variables were not significantly different between the four groups. Endothelium-dependent vasorelaxation induced by a calcium ionophre (A23187) was significantly increased by 4 weeks of pretreatment with losartan. As an indicator of myocardial ischemia, VEGF levels in the ischemic myocardium decreased after 1 and 4 weeks of pretreatment with losartan. Myocardial infarct size was unchanged after 1 day and 1 week pretreatment, but was significantly reduced by 4 weeks of pretreatment with losartan. **Conclusions:** Losartan has time-dependent cardiovascular protective effects. 4 weeks of pretreatment with losartan decreased infarct size and VEGF, and increased endothelial dependent vasorelaxation.

Pretreatment with losartan (*p<0.05, **p<0.01)

Groups	Ang II (pg/ml)	Infarct size (%)	ERP (ms)	VF threshold (mA)	Vasorelax (%)	VEGF
Control	13±3	55±3	31±1	.95±.11	-62±7	1.0
Losartan-1d	53±14	52±7	34±2	.87±.13	-75±9	.93±.11
Losartan-1w	64±14	57±6	28±1	1.15±.47	-76±7	.75±.05*
Losartan-4w	90±37*	38±6*	31±2	1.29±.27	-81±4*	.58±.10**

11:30 a.m.

889-5 **Occlusion of the Infrarenal Aorta Protects the Rat Heart From Infarction: Characterization of a New Humoral Mechanism Responsible for Mediating Remote Preconditioning**

Christof Weinbrenner, Manfred Nelles, Nicole Herzog, László Sárváry, Ruth H. Strasser. *Department of Cardiology, University of Dresden, Dresden, Germany, Department of Cardiology, University of Heidelberg, Heidelberg, Germany*

Background: Ischemic preconditioning (PC) is a powerful tool in reducing infarct size of the. The mechanism of signal transduction of PC, however, is not clear yet. To address the question if the protective signal of PC is transduced by neuronal or humoral factors and if the mechanism is also inducible at a distance we developed an in vivo model of infrarenal occlusion of the aorta (IOA) in the rat. **Methods:** 7 protocols were used: (i) control hearts which underwent 30 min of regional ischemia (Is) followed by 2 hrs of reperfusion (Rep); (ii) classical PC with 3 cycles of repetitive Is and Rep prior to Is; (iii) IOA for 15 min prior to Is and throughout the following experiment (IOA); (iv) IOA for 15 min and Rep of the aorta at the same time as Is started (IOA15); (v-vii) IOA for 5, 10, and 15 min resp., followed by 10 min Rep of the aorta before the beginning of Is (IOA5R, IOA10R, IOA15R). **Results:** Control hearts had an infarct size of 56.5±6.2% of the risk zone whereas PC reduced it to 11.2±4.1% (p<0.001). IOA and IOA15, i.e. IOA without Rep, had no influence on infarct size thus excluding a blood pressure induced effect in the model (43.1±5.2, 52.2±4.4%, resp., p=n.s.). In IOA5R and IOA10R hearts infarct size tended to be smaller than in controls (41.6±2.2, 36.9±8.2%, resp.) whereas in IOA15R hearts infarct size was significantly smaller than in controls (21.4±7.9%, p<0.01). There was a significant time-dependent linear trend for reduction of infarct size between IOA5R, IOA10R, and IOA15R hearts (p<0.005). **Conclusion:** Protection of the heart can be induced at a distance by IOA. Surprisingly this protection is nearly as powerful as PC in reducing infarct size. Reperfusion of the occluded aorta prior to the infarction of the heart is essential, excluding a neuronal factor in the signal mechanism of PC. The power of protection is dependent of the duration of the ischemic period in the lower limb. This suggests a time-dependent production of an ischemia induced protective humoral factor which is transferred to the heart by the blood circulation. This is the first study to clearly characterize that effective remote PC is mediated by a humoral factor. The mediating substance remains to be elucidated.

11:45 a.m.

889-6 **Ischemia and Reperfusion-Induced Changes in Myocardial Contrast and Tissue Doppler Echocardiography Patterns in a Porcine Model of Patchy Myocardial Necrosis Achieved by Acute Partial Occlusion of the Coronaries**

Philippe Garot, Marc Simon, Olivier Pascal, Saleh el Amine, Sophie Benacerraf, Luc Hittinger, Jean-Luc Dubois-Randé, Pascal Guéret, Emmanuel Teiger. *Hopital Henri Mondor, Creteil, France*

Background: Coronary plaque rupture does not always imply complete arterial occlusion. It also may lead to prolonged coronary blood flow reduction. In this setting, changes in myocardial perfusion and contraction remain unclear. **Methods:** 12 closed-chest anesthetized pigs underwent partial occlusion of the right coronary artery using a balloon inflation until distal flow measured by a Doppler guide wire fell by 80%. Myocardial perfusion in the ischemic subendo- (Sendo) and subepicardium (Sepi) was assessed by myocardial contrast echocardiography (MCE) performed with the intracoronary injection of sonicated microbubbles. Peak systolic velocities (PSV) were assessed in the ischemic segment for the Sendo and for the Sepi using M-mode color tissue Doppler echocardiography (short axis view). Both perfusion and contractility were assessed 30 and 90 minutes after ischemia onset and then 10 and 90 minutes after reflow. MCE images were analyzed with the use of the NIH software package (NIH, Bethesda, MD) to determine the peak intensity ratio (PI ratio) defined by the ratio of contrast peak intensity in the enhanced ischemic myocardium and the intensity in the anterior unenhanced wall. The extent of MI was assessed by TTC staining after animal sacrifice. **Results:** Results for PI ratio and PSV in the Sendo and the Sepi are presented as mean ± SD. PSv are expressed as cm.s-1 and I troponin as ng/mL.

	Base	Ischemia 30 min.	Ischemia 90 min.	Reperf. 10 min.	Reperf. 90 min.
PI ratio Sendo	3.21±.48	2.74±.50†	2.02±.55‡	2.78±.43*	3.08±.33
PI ratio Sepi	3.14±.62	3.25±.67	3.22±.71	2.84±.50	3.35±.32
PSV Sendo	4.4±1.7	1.8±1.0‡	1.5±1.3‡	2.8±1.8*	2.5±1.2*
PSV Sepi	2.0±1.0	1.3±.6*	1.5±1.2*	2.1±1.4	1.8±.9
I Troponin	.2±.2	.3±.3	2.1±1.0*	21.1±15.8†	85.9±35.4‡

Conclusion: Severe myocardial ischemia achieved by prolonged partial occlusion of the coronaries is responsible for concomittant and consistent perfusion and contraction abnormalities predominating in the Sendo and yielding to non transmural "patchy" myocardial necrosis.